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Veröffentlicht
*Ohne internationalen Recherchenbericht und erneut zu veröffentlichen nach Erhalt des Berichts.*

(54) Title: EPOTHILONE MINOR CONSTITUENTS

(54) Bezeichnung: EPOTHILON–NEBENKOMPONENTEN

(57) Abstract

The invention relates to compounds which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans–epothilones C1 and C2.

(57) Zusammenfassung

Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 und K und Trans–Epothilone C1 und C2.

*LEDIGLICH ZUR INFORMATION*

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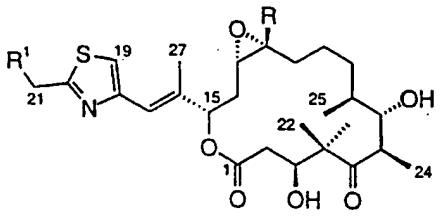
# Epothilon-Nebenkomponenten

Die Erfindung betrifft Verbindungen, die im vorliegenden Zusammenhang als Epothilon-Nebenkomponenten bezeichnet werden, und zwar Verbindungen 5 bis 13 und 16 bis 39. Diese Verbindungen lassen sich durch Fermentation von DSM 6773 gemäß DE 41 38 042.8 gewinnen.

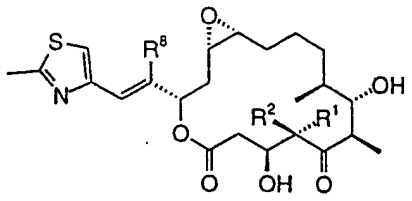
Kenndaten der erfindungsgemäßen Verbindungen sind im folgenden zusammengestellt.

Gewinnung: Die Aufarbeitung eines Rohepothilon-Gemischs, das durch Fermentation von DSM 6773 in einem 900 Liter-Fermentator gewonnen wurde, ist schematisch Fig. 1 bis 2 zu entnehmen.

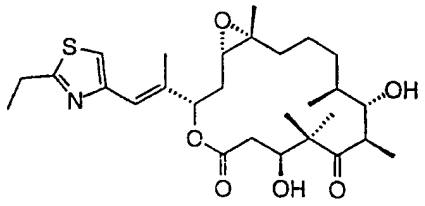
Aktivitäten: vgl. Tab. 1



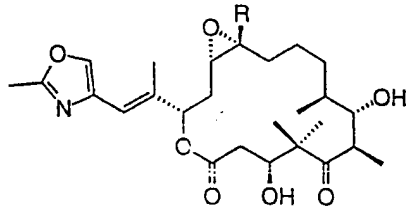
Epothilone A (1) $R^1$ = H; R = H
Epothilone B (2) $R^1$ = H; R = Me
Epothilone E (3) $R^1$ = OH; R = H
Epothilone F (4) $R^1$ = OH; R = Me



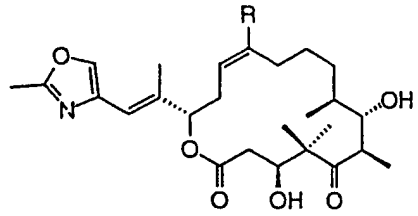
Epothilone $A_1$ (5) $R^1$ = H; $R^2$, $R^8$ = Me
Epothilone $A_2$ (6) $R^2$ = H; $R^1$, $R^8$ = Me
Epothilone $A_8$ (7) $R^8$ = H; $R^1$, $R^2$ = Me
Epothilone $A_9$ (8) $R^1$ = $CH_2OH$; $R^2$, $R^8$ = Me



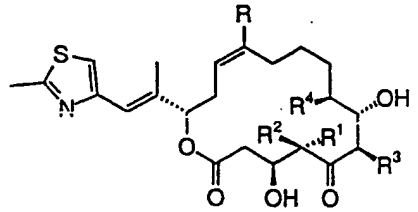
Epothilone $B_{10}$ (9)



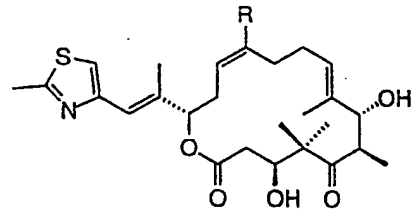
Epothilone $G_1$ (10) R = H
Epothilone $G_2$ (11) R = Me



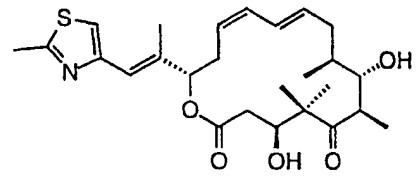
Epothilone $H_1$ (12) R = H
Epothilone $H_2$ (13) R = Me



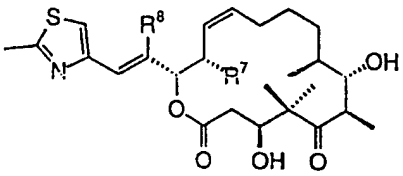
Epothilone C (14) $R^1$, $R^2$, $R^3$, $R^4$ = Me; R = H
Epothilone D (15) $R^1$, $R^2$, $R^3$, $R^4$, R = Me
Epothilone $C_1$ (16) $R^1$ = H; $R^2$, $R^3$, $R^4$ = Me; R = H
Epothilone $D_1$ (17) $R^1$ = H; $R^2$, $R^3$, $R^4$ = Me; R = Me
Epothilone $C_2$ (18) $R^2$ = H; $R^1$, $R^3$, $R^4$ = Me; R = H
Epothilone $D_2$ (19) $R^2$ = H; $R^1$, $R^3$, $R^4$ = Me; R = Me
Epothilone $C_3$ (20) $R^3$ = H; $R^1$, $R^2$, $R^4$ = Me; R = H
Epothilone $C_4$ (21) $R^4$ = H; $R^1$, $R^2$, $R^3$ = Me; R = H



Epothilone $C_5$ (22) R = H
Epothilone $D_5$ (23) R = Me



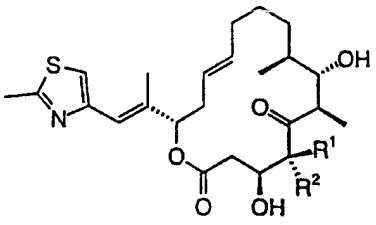
Epothilone $C_6$ (24)



Epothilone $C_7$ **(25)** $R^7 = OH$; $R^8 = Me$

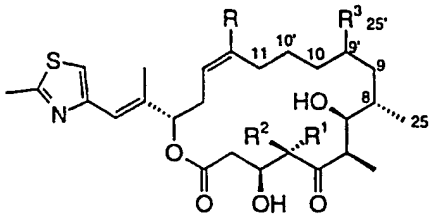
Epothilone $C_8$ **(26)** $R^8, R^7 = H$

Epothilone $C_9$ **(27)** $R^8 = CH_2OH$; $R^7 = H$



trans-Epothilone $C_1$ **(28)** $R^1 = H$; $R^2 = Me$

trans-Epothilone $C_2$ **(29)** $R^2 = H$; $R^1 = Me$



Epothilone $I_1$ **(30)** R, $R^3 = H$; $R^1, R^2 = Me$

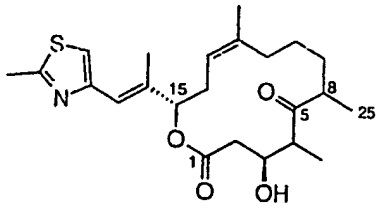
Epothilone $I_2$ **(31)** R = H; $R^1, R^2, R^3 = Me$

Epothilone $I_3$ **(32)** $R^1, R^2, R^3$, R = Me

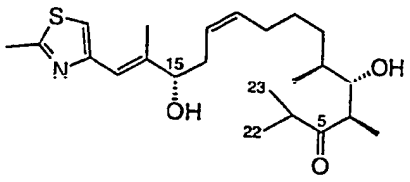
Epothilone $I_4$ **(33)** $R^2$, R = H; $R^1, R^3 = Me$

Epothilone $I_5$ **(34)** $R^2 = H$; $R^1, R^3$, R = Me

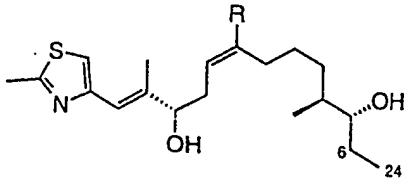
Epothilone $I_6$ **(35)** $R^1 = H$; $R^2, R^3$, R = Me



Epothilone K **(36)**



**(37)**



**(38)** R = H

**(39)** R = Me

**Epothilone $A_1$** (5): colorless amorphous solid; $[\alpha]^{22}_D$ –69 (*c* 0.1, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 208 (19600), 247 (13600); IR (KBr) $\nu_{max}$ 3437, 2959, 2931, 2876, 1732, 1710, 1455, 1259, 978 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 6.95 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.68 (1H, dd, *J* = 4.4, 4.0 Hz, H-15), 4.12 (1H, m, H-3), 3.71 (1H, m, H-7), 3.52 (1H, bs, 7-OH), 3.37 (1H, bd, *J* = 7.5 Hz, 3-OH), 3.21 (1H, dq, *J* = 7.7, 7.0 Hz, H-4), 3.02 (1H, ddd, *J* = 9.2, 4.5, 2.8 Hz, H-13), 2.87 (1H, ddd, *J* = 8.3, 4.5, 3.7 Hz, H-12), 2.78 (1H, dd, *J* = 16.8, 4.3 Hz, H-2a), 2.70 (3H, s, H-21), 2.66 (1H, dq, *J* = 3.9, 7.0 Hz, H-6), 2.65 (1H, dd, *J* = 16.8, 5.2 Hz, H-2b), 2.16 (1H, ddd, *J* = 15.4, 4.4, 2.8 Hz, H-14a), 2.12 (3H, bs, H-27), 1.91 (1H, ddd, *J* = 15.4, 9.2, 4.0 Hz, H-14b), 1.63 (1H, m, H-10a), 1.62 (2H, m, H-11), 1.59 (1H, m, H-9a), 1.52 (1H, m, H-10b), 1.39 (1H, m, H-8), 1.35 (1H, m, H-9b), 1.211 (3H, d, *J* = 7.0 Hz, H-23), 1.207 (3H, d, *J* = 7.0 Hz, H-24), 0.89 (3H, d, *J* = 6.9 Hz, H-25); EIMS *m/z* 479 $[M]^+$ (21), 322 (31), 306 (65), 304 (47), 168 (45), 166 (73), 164 (100), 151 (30), 140 (35); HREIMS *m/z* 479.2317 (calcd. for $C_{27}H_{41}NO_5S$, 479.2342).

**Epothilone $A_2$** (6): colorless amorphous solid; $[\alpha]^{22}_D$ +12.0 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 210 (15100), 248 (15500); IR (KBr) $\nu_{max}$ 3438, 2963, 2929, 2875, 1734, 1706, 1458, 1262, 981 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 6.98 (1H, s, H-19), 6.63 (1H, bs, H-17), 5.40 (1H, dd, *J* = 8.3, 3.4 Hz, H-15), 4.26 (1H, ddd, *J* = 8.5, 4.8, 4.7 Hz, H-3), 3.85 (1H, dd, *J* = 7.9,

2.6 Hz, H-7), 3.54 (1H, bs, 3-OH), 3.09 (1H, dq, $J$ = 4.8, 7.0 Hz, H-4), 3.01 (1H, ddd, $J$ = 8.3, 4.8, 4.6 Hz, H-13), 2.98 (1H, dq, $J$ = 7.9, 7.0 Hz, H-6), 2.89 (1H, ddd, $J$ = 6.7, 4.6, 4.4 Hz, H-12), 2.68 (3H, s, H-21), 2.60 (1H, dd, $J$ = 15.1, 8.5 Hz, H-2a), 2.52 (1H, bs, 7-OH), 2.50 (1H, dd, $J$ = 15.1, 4.7 Hz, H-2b), 2.18 (1H, ddd, $J$ = 15.0, 4.8,3.4 Hz, H-14a), 2.11 (3H, d, $J$ = 1.3 Hz, H-27), 1.82 (1H, ddd, $J$ = 15.0, 8.3, 8.1 Hz, H-14b), 1.63 (1H, m, H-8), 1.61 (2H, m, H-11a and H-10a), 1.46 (1H, m, H-11b), 1.39 (2H, m, H-9), 1.31 (1H, m, H-10b), 1.22 (3H, d, $J$ = 7.0 Hz, H-24), 1.15 (3H, d, $J$ = 7.0 Hz, H-22), 1.01 (3H, d, $J$ = 6.9 Hz, H-25); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 216.2 (s, C-5), 170.1 (s, C-1), 164.9 (s, C-20), 152.0 (s, C-18), 137.0 (s, C-16), 120.3 (d, C-17), 116.5 (d, C-19), 76.7 (d, C-15), 75.6 (d, C-7), 69.1 (d, C-3), 57.1 (d, C-12), 54.3 (d, C-13), 50.3 (d, C-4), 49.6 (d, C-6), 39.4 (t, C-2), 35.5 (d, C-8), 32.2 (t, C-14), 29.6 (t, C-9), 27.6 (t, C-11), 23.9 (t, C-10), 19.2 (q, C-21), 18.0 (q, C-25), 15.6 (q, C-27), 13.9 (q, C-24), 12.4 (q, C-22); EIMS *m/z* 479 $[M]^+$ (18), 322 (38), 306 (78), 304 (59), 168 (48), 166 (96), 164 (100), 151 (33), 140 (38); HREIMS *m/z* 479.2318 (calcd. for $C_{27}H_{41}NO_5S$, 479.2342).

**Epothilone $A_5$ (7)**: colorless amorphous solid; $[\alpha]^{22}_D$ –76.2 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 210 (15300), 248 (15500); IR (KBr) $\nu_{max}$ 3440, 2967, 2932, 2876, 1736, 1691, 1467, 1252, 979 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 6.95 (1H, s, H-19), 6.64 (1H, dd, $J$ = 15.6, 0.9 Hz, H-17), 6.52 (1H, dd, $J$ = 15.6, 6.6 Hz, H-16), 5.68 (1H, dddd, $J$ = 7.8, 6.6, 3.2, 0.9 Hz, H-15), 4.11 (1H, ddd, $J$ = 10.1, 6.6, 3.5 Hz, H-3), 3.78 (1H, ddd, $J$ = 5.2, 3.2, 3.2 Hz, H-7), 3.66 (1H, d, $J$ = 6.6 Hz, 3-OH), 3.23 (1H, dq, $J$ = 5.2, 6.9 Hz, H-6), 3.08 (1H, ddd, $J$ = 7.3, 5.5 ,4.1 Hz, H-13), 2.90 (1H, ddd, $J$ = 6.6, 4.6, 4.1 Hz, H-12), 2.69 (3H, s, H-21), 2.52 (1H, dd, $J$ = 14.7, 10.1 Hz, H-2a), 2.44 (1H, bd, $J$ = 3.2 Hz, 7-OH), 2.41 (1H, dd, $J$ = 14.7, 3.5 Hz, H-2b), 2.10

(1H, ddd, $J$ = 15.0, 5.5, 3.2 Hz, H-14a), 1.90 (1H, ddd, $J$ = 15.0, 7.8, 7.3 Hz, H-14b), 1.71 (1H, m, H-8), 1.65 (1H, m, H-11a), 1.50 (1H, m, H-10a), 1.47 (1H, m, H-11b), 1.40 (2H, m, H-9), 1.39 (1H, m, H-10b), 1.33 (3H, s, H-23), 1.16 (3H, d, $J$ = 6.9 Hz, H-24), 1.08 (3H, s, H-22), 0.98 (3H, d, $J$ = 7.0 Hz, H-25); $^{13}$C NMR ($CDCl_3$, 75 MHz) δ 220.3 (s, C-5), 170.7 (s, C-1), 166.5 (s, C-20), 152.2 (s, C-18), 128.4 (d, C-16), 125.9 (d, C-17), 116.4 (d, C-19), 75.0 (d, C-7), 73.6 (d, C-3), 72.7 (d, C-15), 57.3 (d, C-12), 54.1 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.9 (t, C-2), 36.3 (d, C-8), 32.5 (t, C-14), 30.3 (t, C-9), 26.7 (t, C-11), 24.0 (t, C-10), 21.3 (q, C-23), 21.0 (q, C-22), 19.3 (q, C-21), 17.1 (q, C-25), 14.5 (q, C-24); **EIMS** ***m/z*** **479 [M]$^+$ XXX;** HRDCIMS *m/z* 480.2401 (calcd. for $C_{25}H_{38}NO_6S$, 480.2401).

**Epothilone $A_9$ (8):** colorless amorphous solid; $[\alpha]^{22}_D$ –37.6 (*c* 0.5, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 211 (15500), 253 (14100); IR (KBr) $\nu_{max}$ 3423, 2965, 2932, 2877, 1736, 1690, 1463, 1249, 1014, 979 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.10 (1H, s, H-19), 6.72 (1H, dd, $J$ = 10.7, 4.3 Hz, 27-OH), 6.60 (1H, bs, H-17), 5.69 (1H, dd, $J$ = 11.6, 2.0 Hz, H-15), 5.59 (1H, d, $J$ = 6.6 Hz, 3-OH), 4.49 (1H, ddd, $J$ = 12.9, 4.3, 1.2 Hz, H-27a), 4.27 (1H, ddd, $J$ = 11.6, 6.6, 2.9 Hz, H-3), 4.11 (1H, ddd, $J$ = 12.9, 10.7, 1.0 Hz, H-27b), 3.71 (1H, ddd, $J$ = 4.8, 3.0, 2.8 Hz, H-7), 3.17 (1H, dq, $J$ = 3.0, 6.8 Hz, H-6), 3.04 (1H, ddd, $J$ = 9.7, 3.6, 2.2 Hz, H-13), 2.93 (1H, bs, 7-OH), 2.91 (1H, ddd, $J$ = 9.7, 3.6, 2.7 Hz, H-12), 2.72 (3H, s, H-21), 2.48 (1H, dd, $J$ = 14.2, 11.6 Hz, H-2a), 2.11 (1H, dd, $J$ = 14.2, 2.9 Hz, H-2b), 2.03 (1H, ddd, $J$ = 14.7, 2.2, 2.0 Hz, H-14a), 1.86 (1H, m, H-11a), 1.85 (1H, m, H-14b), 1.79 (1H, m, H-8), 1.52 (1H, m, H-10a), 1.37 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.36 (1H, m, H-11b), 1.19 (3H, d, $J$ = 6.8 Hz, H-24), 1.02 (3H, d, $J$ = 7.1 Hz, H-25), 1.00 (3H, s, H-22); $^{13}$C NMR ($CDCl_3$, 75 MHz) δ 220.5 (s, C-5),

170.2 (s, C-1), 167.5 (s, C-20), 150.7 (s, C-18), 138.9 (s, C-16), 125.2 (d, C-17), 119.5 (d, C-19), 76.7 (d, C-15), 73.4 (d, C-7), 70.4 (d, C-3), 57.7 (d, C-12), 57.2 (t, C-27), 55.3 (d, C-13), 54.2 (s, C-4), 41.3 (d, C-6), 40.7 (t, C-2), 37.5 (d, C-8), 31.8 (t, C-14), 31.2 (t, C-9), 28.0 (t, C-11), 23.7 (q, C-23), 23.2 (t, C-10), 19.2 (q, C-21), 16.8 (q, C-22), 15.8 (q, C-25), 13.5 (q, C-24); EIMS *m/z* 509 $[M]^+$ (9), 491 (4), 322 (28), 321 (25), 180 (45), 167 (40), 166 (100), 165 (49), 154 (47), 138 (33); HREIMS *m/z* 509.2467 (calcd. for $C_{26}H_{39}NO_7S$, 509.2447).

**Epothilone $B_{10}$ (9)**: colorless amorphous solid; $[\alpha_D]^{22}$ **–27 (*c* 0.15, MeOH); UV** (MeOH) $\lambda_{max}$ **nm (ε) 212 (15800), 247 (12500);** IR (KBr) $\nu_{max}$ 3434, 2962, 2930, 2876, 2858, 1733, 1692, 1461, 1259, 1052, 981 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz) δ 6.99 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.42 (1H, dd, *J* = 8.0, 3.0 Hz, H-15), 4.25 (1H, ddd, *J* = 9.5, 6.3, 2.8 Hz, H-3), 4.23 (1H, bs, 3-OH), 3.77 (1H, ddd, *J* = 4.0, 3.9, 3.8 Hz, H-7), 3.30 (1H, dq, *J* = 4.0, 6.9 Hz, H-6), 3.01 (2H, q, *J* = 7.6 Hz, H-21), 2.81 (1H, dd, *J* = 7.7, 4.6 Hz, H-13), 2.68 (1H, bs, 7-OH), 2.54 (1H, dd, *J* = 13.9, 9.5 Hz, H-2a), 2.36 (1H, dd, *J* = 13.9, 2.8 Hz, H-2b), 2.11 (1H, ddd, *J* = 15.3, 4.6, 3.0 Hz, H-14a), 2.09 (3H, s, H-27), 1.91 (1H, ddd, *J* = 15.3, 8.0, 7.7 Hz, H-14b), 1.74 (1H, m, H-8), 1.73 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.41 (1H, m, H-11b), 1.39 (3H, t, *J* = 7.6 Hz, H-28), 1.38 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.28 (3H, s, H-26), 1.17 (3H, d, *J* = 6.9 Hz, H-24), 1.09 (3H, s, H-22), 1.01 (3H, d, *J* = 7.0 Hz, H-25); EIMS *m/z* 521 $[M]^+$ (22), 449 (7), 350 (18), 334 (57), 248 (16), 234 (27), 196 (41), 182 (59), 180 (96), 178 (100), 166 (44), 154 (44); HREIMS *m/z* 521.2808 (calcd. for $C_{28}H_{43}NO_6S$, 521.2811).

**Epothilone $G_1$ (10)**: colorless amorphous solid; $[\alpha]^{22}_D$ –39.7 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 203 (15200), 236 (15100); IR (KBr) $\nu_{max}$ 3456, 2962, 2933, 2876, 1736,

1691, 1585, 1466, 1262, 980 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.47 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.42 (1H, dd, *J* = 8.3, 2.9 Hz, H-15), 4.11 (1H, ddd, *J* = 10.1, 6.1, 3.4 Hz, H-3), 3.78 (1H, bddd, *J* = 5.2, 3.5, 3.5 Hz, H-7), 3.63 (1H, bd, *J* = 6.1 Hz, 3-OH), 3.21 (1H, dq, *J* = 5.2, 7.0 Hz, H-6), 3.00 (1H, ddd, *J* = 7.7, 4.8, 4.2 Hz, H-13), 2.88 (1H, ddd, *J* = 7.1, 4.2, 4.2 Hz, H-12), 2.53 (1H, dd, *J* = 14.8, 10.1 Hz, H-2a), 2.51 (1H, bd, *J* = 3.5 Hz, 7-OH), 2.43 (1H, dd, *J* = 14.8, 3.4 Hz, H-2b), 2.43 (3H, s, H-21), 2.07 (1H, ddd, *J* = 15.1, 4.8, 2.9 Hz, H-14a), 1.99 (3H, d, *J* = 1.3 Hz, H-27), 1.86 (1H, ddd, *J* = 15.1, 8.3, 7.7 Hz, H-14b), 1.71 (1H, m, H-8), 1.69 (1H, m, H-11a), 1.53 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.40 (3H, m, H-9 and H-10b), 1.34 (3H, s, H-23), 1.16 (3H, d, *J* = 7.0 Hz, H-24), 1.09 (3H, s, H-22), 0.99 (3H, d, *J* = 6.9 Hz, H-25); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ 220.1 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.7 (s, C-16), 135.9 (d, C-19), 116.4 (d, C-17), 76.4 (d, C-15), 74.9 (d, C-7), 73.7 (d, C-3), 57.4 (d, C-12), 54.4 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.8 (t, C-2), 36.2 (d, C-8), 31.4 (t, C-14), 30.4 (t, C-9), 27.0 (t, C-11), 23.9 (t, C-10), 21.3 (q, C-23), 21.2 (q, C-22), 17.2 (q, C-25), 15.8 (q, C-27), 14.4 (q, C-24), 13.8 (q, C-21); EIMS *m/z* 477 $[M]^+$ (4), 405 (7), 290 (40), 152 (39), 150 (100), 148 (23), 124 (23); HREIMS *m/z* 477.2684 (calcd. for $C_{26}H_{39}NO_7$, 477.2727).

**Epothilone $G_2$ (11):** colorless amorphous solid; $[\alpha]^{22}_D$ –22.6 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 202 (21500), 236 (14800); IR (KBr) $\nu_{max}$ 3456, 2965, 2934, 2877, 1737, 1690, 1586, 1464, 1250, 980 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.48 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.43 (1H, dd, *J* = 7.1, 3.6 Hz, H-15), 4.12 (1H, ddd, *J* = 9.9, 6.4, 3.4 Hz, H-3), 3.77 (1H, ddd, *J* = 4.7, 4.4, 4.1 Hz, H-7), 3.83 (1H, bd, *J* = 6.4 Hz, 3-OH), 3.30 (1H, dq, *J* = 4.7, 6.9

Hz, H-6), 2.78 (1H, dd, $J$ = 7.0, 5.4 Hz, H-13), 2.54 (1H, dd, $J$ = 14.3, 9.9 Hz, H-2a), 2.51 (1H, bd, $J$ = 4.1 Hz, 7-OH), 2.44 (3H, s, H-21), 2.40 (1H, dd, $J$ = 14.3, 3.4 Hz, H-2b), 2.03 (1H, ddd, $J$ = 15.2, 5.4, 3.6 Hz, H-14a), 2.00 (3H, d, $J$ = 1.3 Hz, H-27), 1.92 (1H, ddd, $J$ = 15.1, 7.1, 7.0 Hz, H-14b), 1.71 (1H, m, H-8), 1.68 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.39 (3H, m, H-9 and H-10b), 1.35 (3H, s, H-23), 1.26 (3H, s, H-26), 1.16 (3H, d, $J$ = 6.9 Hz, H-24), 1.07 (3H, s, H-22), 0.99 (3H, d, $J$ = 7.0 Hz, H-25); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 220.7 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.5 (s, C-16), 135.9 (d, C-19), 116.3 (d, C-17), 76.6 (d, C-15), 74.6 (d, C-7), 73.5 (d, C-3), 61.3 (s, C-12), 61.1 (d, C-13), 52.7 (s, C-4), 43.4 (d, C-6), 39.0 (t, C-2), 36.5 (d, C-8), 32.0 (t, C-11), 31.8 (t, C-14), 30.8 (t, C-9), 22.8 (t, C-10), 22.9 (q, C-26), 21.0 (q, C-23), 20.8 (q, C-22), 17.2 (q, C-25), 15.9 (q, C-27), 14.1 (q, C-24), 13.8 (q, C-21); EIMS *m/z* 491[M]$^+$ (21), 419 (6), 320 (18), 304 (39), 166 (42), 152 (57), 150 (100), 149 (44), 148 (58), 124 (35), 109 (33); HREIMS *m/z* 491.2878 (calcd. for $C_{27}H_{41}NO_7$, 491.2883).

**Epothilone $H_1$ (12)**: colorless amorphous solid; $[\alpha]^{22}_D$ −84.2 (*c* 0.2, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 203 (19600), 237 (12000); IR (KBr) $\nu_{max}$ 3436, 2933, 2880, 2860, 1734, 1688, 1585, 1251, 1007 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.47 (1H, s, H-19), 6.31 (1H, bs, H-17), 5.43 (1H, ddd, $J$ = 10.6, 10.2, 4.5 Hz, H-12), 5.36 (1H, dddd, $J$ = 10.6, 9.6, 5.0, 1.3 Hz, H-13), 5.30 (1H, dd, $J$ = 9.9, 2.0 Hz, H-15), 4.16 (1H, ddd, $J$ = 11.2, 5.3, 2.8 Hz, H-3), 3.73 (1H, ddd, $J$ = 3.9, 2.5, 2.3 Hz, H-7), 3.12 (1H, dq, $J$ = 2.3, 6.9 Hz, H-6), 2.92 (1H, d, $J$ = 2.5 Hz, 7-OH), 2.91 (1H, d, $J$ = 5.3 Hz, 7-OH), 2.66 (1H, ddd, $J$ = 15.1, 9.9, 9.6 Hz, H-14a), 2.50 (1H, dd, $J$ = 15.4, 11.2 Hz, H-2a), 2.43 (3H, s, H-21), 2.37 (1H, dd, $J$ = 15.4, 2.8 Hz, H-2b), 2.23

(1H, m, H-14b), 2.18 (1H, m, H-11a), 2.01 (1H, m, H-11b), 2.08 (3H, d, $J$ = 1.3 Hz, H-27), 1.74 (1H, m, H-8), 1.65 (1H, m, H-10a),1.33 (1H, m, H-9a), 1.31 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.17 (3H, d, $J$ = 6.9 Hz, H-24), 1.08 (3H, s, H-22), 0.99 (3H, d, $J$ = 7.1 Hz, H-25); $^{13}$C NMR, see Table 1; EIMS *m/z* 461 $[M]^+$ (6), 310 (5), 274 (10), 273 (7), 171 (63), 152 (100), 148 (18), 111 (15); HREIMS *m/z* 461.2743 (calcd. for $C_{26}H_{39}NO_6$, 461.2777).

**Epothilone $E_2$ (13):** colorless amorphous solid; $[\alpha]^{22}_D$ –44.4 (*c* 0.25, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 203 (14500), 236 (12200); IR (KBr) $\nu_{max}$ 3436, 2967, 2935, 2880, 1734, 1690, 1586, 1251, 1007 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.46 (1H, s, H-19), 6.30 (1H, bs, H-17), 5.23 (1H, dd, $J$ = 9.8, 2.1 Hz, H-15), 5.12 (1H, dd, $J$ = 10.1, 5.3 Hz, H-13), 4.20 (1H, ddd, $J$ = 10.8, 5.7, 2.9 Hz, H-3), 3.71 (1H, ddd, $J$ = 3.8, 2.6, 2.6 Hz, H-7), 3.14 (1H, dq, $J$ = 2.6, 6.9 Hz, H-6), 2.93 (d, $J$ = 5.7 Hz, 3-OH), 2.90 (1H, bd, $J$ = 2.6 Hz, 7-OH), 2.62 (1H, ddd, $J$ = 15.1, 9.8, 9.8 Hz, H-14a), 2.46 (1H, dd, $J$ = 15.1, 10.8 Hz, H-2a), 2.43 (3H, s, H-21), 2.32 (1H, dd, $J$ = 15.1, 2.9 Hz, H-2b), 2.29 (1H, m, H-11a), 2.19 (1H, bd, $J$ = 15.1 Hz, H-14b), 1.97 (3H, d, $J$ = 1.3 Hz, H-27), 1.87 (1H, m, H-11b), 1.73 (1H, m, H-8), 1.67 (1H, m, H-10a), 1.65 (3H, bs, H-26), 1.32 (3H, s, H-23), 1.26 (2H, m, H-9), 1.24 (1H, m, H-10b), 1.18 (3H, d, $J$ = 6.9 Hz, H-24), 1.07 (3H, s, H-22), 1.00 (3H, d, $J$ = 7.0 Hz, H-25); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 220.6 (s, C-5), 170.3 (s, C-1), 161.0 (s, C-20), 138.6 (s, C-12), 138.4 (s, C-16), 137.5 (s, C-18), 135.6 (d, C-19), 120.8 (d, C-13), 115.8 (d, C-17), 78.9 (d, C-15), 74.3 (d, C-7), 72.7 (d, C-3), 53.3 (s, C-4), 42.0 (d, C-6), 39.6 (t, C-2), 38.6 (d, C-8), 32.4 (t, C-14), 31.9 (t, C-9), 31.6 (t, C-11), 25.6 (t, C-10), 23.0 (q, C-26), 22.8 (q, C-23), 18.8 (q, C-22), 16.1 (q, C-27), 15.9 (q, C-25), 13.8 (q, C-21), 13.6 (q, C-24); EIMS *m/z* 475 $[M]^+$ (11), 288 (9), 287 (5), 188(7), 171 (32), 152 (100),

111 (10); HREIMS *m/z* 475.2913 (calcd. for $C_{27}H_{41}NO_6$, 475.2934).

**Epothilone $C_1$ (16):** colorless amorphous solid; $[\alpha]^{22}_D$ −114.0 (*c* 10.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 211 (16500), 248 (12500); IR (KBr) $\nu_{max}$ 3440, 2933, 2877, 2858, 1730, 1708, 1457, 1244, 981 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.96 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.47 (1H, dd, *J* = 9.2, 3.0 Hz, H-15), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 4.40 (1H, ddd, *J* = 6.2, 6.1, 6.1 Hz, H-3), 3.69 (1H, dd, *J* = 5.7, 3.6 Hz, H-7), 3.01 (1H, dq, *J* = 5.7, 6.9 Hz, H-6), 3.01 (1H, bs, 3-OH), 2.84 (1H, dq, *J* = 5.2, 7.0 Hz, H-4), 2.68 (3H, s, H-21), 2.66 (1H, ddd, *J* = 16.4, 9.2, 7.3 Hz, H-14a), 2.64 (1H, dd, *J* = 15.9, 7.1 Hz, H-2a), 2.54 (1H, dd, *J* = 15.9, 6.1 Hz, H-2b), 2.38 (1H, bd, *J* = 16.4 Hz, H-14b), 2.35 (1H, bs, 7-OH), 2.07 (3H, bs, H-27), 2.03 (2H, m, H-11), 1.62 (1H, m, H-10a), 1.53 (1H, m, H-8), 1.35 (1H, m, H-9a), 1.22 (1H, m, H-9b), 1.19 (3H, d, *J* = 6.9 Hz, H-24), 1.14 (3H, d, *J* = 6.9 Hz, H-23), 1.10 (1H, m, H-10b), 0.95 (3H, d, *J* = 6.9 Hz, H-25); $^{13}C$ NMR, see Table 1; EIMS *m/z* 463 $[M]^+$ (5), 324 (8), 290 (8), 204 (7), 168 (100), 164 (15), 139 (36); HREIMS *m/z* 463.2381 (calcd. for $C_{25}H_{37}NO_5S$, 463.2392).

**Epothilone $D_1$ (17)**: colorless amorphous solid; $[\alpha]^{22}_D$ −118.6 (*c* 0.5, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 208 (18300), 249 (11900); IR (KBr) $\nu_{max}$ 3439, 2965, 2934, 2877, 1729, 1707, 1456, 1250, 980 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.98 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.51 (1H, dd, *J* = 9.5, 3.4 Hz, H-15), 5.16 (1H, dd, *J* = 8.0, 4.2 Hz, H-13), 4.42 (1H, ddd, *J* = 7.1, 6.3, 5.5 Hz, H-3), 3.70 (1H, dd, *J* = 6.5, 2.9 Hz, H-7), 3.07 (1H, dq, *J* = 6.5, 6.9 Hz, H-6), 2.95 (1H, dq, *J* = 4.7, 7.0 Hz, H-4), 2.71 (3H, s, H-21), 2.69 (1H, dd, *J* = 16.0, 6.3 Hz, H-2a), 2.64 (1H, m, H-14a), 2.59 (1H, dd, *J* = 16.0, 7.1 Hz, H-2b), 2.46 (1H, bs, 3-OH), 2.38 (1H, bd, *J* = 16.0 Hz, H-14b), 2.19 (1H, ddd, *J* = 13.3, 8.6, 5.7 Hz, H-11a), 2.10 (3H, d, *J* = 1.4 Hz, H-27), 2.02 (1H, bs, 7-OH), 1.91 (1H, ddd, *J* = 13.3, 6.0, 6.0 Hz, H-11b), 1.68 (1H, m, H-10a), 1.66 (3H, bs, H-26), 1.53 (1H, m, H-8), 1.37 (1H, m, H-9a), 1.26 (1H, m, H-9b), 1.24 (3H, d, *J* = 6.9 Hz, H-24), 1.19 (1H, m, H-10b), 1.14 (3H, d. *J* = 7.0, H-23), 0.99 (3H, d, *J* = 6.9 Hz, H-25); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ 217.0 (s, C-5), 169.7 (s, C-1), 165.0 (s, C-20), 152.2 (s, C-18), 138.5 (s, C-12), 137.7 (s, C-16), 120.7 (d, C-13), 120.1 (d, C-17), 116.3 (d, C-19), 78.8 (d, C-15), 77.2 (d, C-7), 67.7 (d, C-3), 52.1 (d, C-4), 46.5 (d, C-6), 40.6 (t, C-2), 37.6 (d, C-8), 32.3 (t, C-14), 31.8 (t, C-11), 29.5(t, C-9), 25.5 (t, C-10), 23.1 (q, C-26), 19.2 (q, C-21), 15.5 (q, C-27), 16.6 (q, C-25), 14.5 (q, C-24), 9.7 (q, C-23); EIMS *m/z* 477 $[M]^+$ (13), 304 (19), 303 (31), 218 (40), 204 (41), 168 (100), 164 (45), 157 (25), 139 (18); HREIMS *m/z* 477.2544 (calcd. for $C_{26}H_{39}NO_5S$, 477.2549).

**Epothilone $C_2$ (18)**: colorless amorphous solid; $[\alpha]^{22}_D$ −11.6 (*c* 10.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 212 (15500), 249 (12100); IR (KBr) $\nu_{max}$ 3428, 2962, 2929, 2877, 2859, 1734, 1705, 1460, 1251, 982 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.99 (1H, s, H-19), 6.66 (1H,

bs, H-17), 5.55 (1H, ddd, $J$ = 10.4, 9.2, 6.1 Hz, H-12), 5.38 (1H, ddd, $J$ = 10.4, 9.3, 6.2 Hz, H-13), 5.22 (1H, dd, $J$ = 8.8, 2.8 Hz, H-15), 4.42 (1H, dddd, $J$ = 9.4, 5.6, 4.2, 4.1 Hz, H-3), 3.93 (1H, d, $J$ = 5.6 Hz, 3-OH), 3.86 (1H, m, H-7), 3.15 (1H, bs, 7-OH), 3.12 (1H, dq, $J$ = 4.2, 7.0 Hz, H-4), 3.00 (1H, dq, $J$ = 6.9, 7.0 Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dddd, $J$ = 15.1, 9.3, 8.8, 0.8 Hz, H-14a), 2.58 (1H, dd, $J$ = 15.4, 9.4 Hz, H-2a), 2.38 (1H, dd, $J$ = 15.4, 4.1 Hz, H-2b), 2.31 (1H, ddd, $J$ = 15.1, 6.2, 2.8 Hz, H-14b), 2.08 (3H, d, $J$ = 1.3 Hz, H-27), 2.15 (1H, m, H-11a), 2.04 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.59 (1H, m, H-10a), 1.43 (1H, m, H-9a), 1.31 (1H, m, H-9b), 1.26 (3H, d, $J$ = 7.0 Hz, H-24), 1.15 (3H, d, $J$ = 7.0 Hz, H-23), 1.11 (1H, m, H-10b), 1.00 (3H, d, $J$ = 6.9 Hz, H-25); $^{13}$C NMR, see Table 1; EIMS *m/z* 463 $[M]^+$ (7), 324 (7), 306 (8), 290 (17), 168 (100), 164 (14), 139 (27); HREIMS *m/z* 463.2392 (calcd. for $C_{25}H_{37}NO_5S$, 463.2392).

**Epothilone D** (19): colorless amorphous solid; $[\alpha]^{22}_D$ −12.5 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 210 (15400), 248 (11200); IR (KBr) $\nu_{max}$ 3436, 2965, 2930, 2877, 1732, 1705, 1458, 1253, 980 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 6.97 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.18 (1H, dd, $J$ = 7.9, 4.9 Hz, H-15), 5.18 (1H, ddd, $J$ = 9.6, 5.4, 1.0 Hz, H-13), 4.27 (1H, m, H-3), 3.88 (1H, dd, $J$ = 5.6, 4.6 Hz, H-7), 3.19 (1H, bs, 3-OH), 3.07 (1H, dq, $J$ = 4.3, 7.0 Hz, H-4), 2.95 (1H, dq, $J$ = 5.6, 7.0 Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd, $J$ = 14.9, 7.8 Hz, H-2a), 2.56 (1H, ddd, $J$ = 14.7, 9.6, 7.9 Hz, H-14a), 2.43 (1H, dd, $J$ = 14.9, 5.6 Hz, H-2b), 2.38 (1H, bs, 7-OH), 2.26 (1H, ddd, $J$ = 14.5, 5.4, 4.9 Hz, H-14b), 2.19 (1H, ddd, $J$ = 13.0, 10.4, 5.4 Hz, H-11a), 2.10 (3H, d, $J$ = 1.4 Hz, H-27), 1.95 (1H, ddd, $J$ = 13.0, 10.3, 5.3 Hz, H-11b), 1.72 (1H, m, H-8), 1.68 (3H, bs, H-26), 1.61 (1H, m, H-10a), 1.39 (2H, m, H-9), 1.21 (1H, m, H-10b),

1.19 (3H, d, $J$ = 6.9 Hz, H-24), 1.17 (3H, d. $J$ = 7.0, H-22), 1.00 (3H, d, $J$ = 6.9 Hz, H-25); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 216.8 (s, C-5), 170.4 (s, C-1), 164.9 (s, C-20), 152.3 (s, C-18), 139.8 (s, C-12), 137.5 (s, C-16), 120.5 (d, C-17), 119.2 (d, C-13), 116.3 (d, C-19), 80.0 (d, C-15), 74.3 (d, C-7), 69.7 (d, C-3), 48.6 (d, C-4), 48.4 (d, C-6), 39.9 (t, C-2), 36.6 (d, C-8), 32.2 (t, C-14), 32.7 (t, C-11), 30.9 (t, C-9), 26.0 (t, C-10), 23.6 (q, C-26), 19.2 (q, C-21), 15.4 (q, C-27), 17.1 (q, C-25), 12.4 (q, C-24),12.7 (q, C-23); EIMS *m/z* 477 $[M]^+$ (22), 304 (19), 303 (17), 218 (22), 204 (25), 168 (100), 164 (28), 157 (31), 139 (21); HREIMS *m/z* 477.2545 (calcd. for $C_{26}H_{39}NO_5S$, 477.2549).

**Epothilone $C_3$ (20)**: colorless amorphous solid; $[\alpha]^{22}_D$ –62.1 (*c* 5.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 212 (16200), 248 (12300); IR (KBr) $\nu_{max}$ 3432, 2928, 2878, 2858, 1736, 1698, 1252, 1040 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz) δ 6.95 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.44 (1H, ddd, $J$ = 10.9, 10.3, 5.4 Hz, H-12), 5.33 (1H, ddd, $J$ = 10.9, 9.3, 4.6 Hz, H-13), 5.23 (1H, dd, $J$ = 9.5, 2.2 Hz, H-15), 4.36 (1H, ddd, $J$ = 11.3, 5.6, 2.3 Hz, H-3), 4.04 (1H, d, $J$ = 5.6 Hz, 3-OH), 3.93 (1H, ddd, $J$ = 9.5, 2.3, 1.4 Hz, H-7), 3.56 (1H, bd, $J$ = 2.3 Hz, 7-OH), 2.70 (1H, dd, $J$ = 18.0, 1.4 Hz, H-6a), 2.67 (3H, s, H-21), 2.61 (1H, ddd, $J$ = 15.3, 9.5, 9.3 Hz, H-14a), 2.38 (1H, dd, $J$ = 14.3, 11.3 Hz, H-2a), 2.36 (1H, dd, $J$ = 18.0, 9.5 Hz, H-6b), 2.28 (1H, bd, $J$ = 15.3 Hz, H-14b), 2.12 (1H, m, H-11a), 2.06 (1H, dd, $J$ = 14.3, 2.3 Hz, H-2b), 2.03 (3H, d, $J$ = 1.3 Hz, H-27), 1.96 (1H, m, H-11b), 1.75 (1H, m, H-8), 1.54 (1H, m, H-10a),1.26 (1H, m, H-9a), 1.25 (3H, s, H-23), 1.17 (1H, m, H-10b), 1.15 (1H, m, H-9b), 1.03 (3H, s, H-22), 0.91 (3H, d, $J$ = 6.8 Hz, H-25); $^{13}$C NMR, see Table 1; EIMS *m/z* 463 $[M]^+$ (28), 290 (14), 168 (100), 164 (36), 157 (44), 151 (25); HREIMS *m/z* 463.2379 (calcd. for $C_{25}H_{37}NO_5S$, 463.2392).

**Epothilone $C_4$ (21):** colorless amorphous solid; $[\alpha]^{22}_D$ –75.6 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 212 (17200), 248 (12500); IR (KBr) $\nu_{max}$ 3434, 2974, 2932, 2859, 1735, 1686, 1252, 1046 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.96 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 5.26 (1H, dd, *J* = 9.6, 2.3 Hz, H-15), 4.41 (1H, ddd, *J* = 11.4, 5.8, 2.5 Hz, H-3), 3.78 (1H, m, H-7), 3.70 (1H, bs, 3-OH), 3.46 (1H, d, *J* = 0.9 Hz, 7-OH), 3.01 (1H, dq, *J* = 0.5, 7.0 Hz, H-6), 2.69 (3H, s, H-21), 2.66 (1H, ddd, *J* = 15.3, 9.6, 8.8 Hz, H-14a), 2.47 (1H, dd, *J* = 14.5, 11.4 Hz, H-2a), 2.29 (1H, m, H-14b), 2.25 (1H, dd, *J* = 14.5, 2.5 Hz, H-2b), 2.24 (1H, m, H-11a), 2.07 (3H, d, *J* = 1.4 Hz, H-27), 1.96 (1H, m, H-11b), 1.51 (2H, m, H-8), 1.44 (2H, m, H-10),1.37 (2H, m, H-9), 1.32 (3H, s, H-23), 1.17 (3H, d, *J* = 7.0 Hz, H-24), 1.07 (3H, s, H-22); $^{13}C$ NMR, see Table 1; EIMS *m/z* 463 $[M]^+$ (7), 276 (15), 171 (33), 168 (100), 164 (23), 151 (22), 111 (13); HREIMS *m/z* 463.2373 (calcd. for $C_{25}H_{37}NO_5S$, 463.2392).

**Epothilone $C_5$ (22):** colorless amorphous solid; $[\alpha]^{22}_D$ –158.2 (*c* 0.5, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 205 (19500), 247 (12700); IR (KBr) $\nu_{max}$ 3447, 2972, 2927, 1737, 1690, 1450, 1252, 1181, 986 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 6.93 (1H, s, H-19), 6.48 (1H, bs, H-17), 5.48 (1H, ddd, *J* = 10.7, 6.2, 6.2 Hz, H-12), 5.39 (1H, m, H-13), 5.37 (1H, m, H-9), 5.34 (1H, dd, *J* = 8.0, 2.3 Hz, H-15), 4.29 (1H, dd, *J* = 6.0, 2.6 Hz, H-7), 4.09 (1H, ddd, *J* = 10.8, 7.1, 2.9 Hz, H-3), 3.59 (1H, d, *J* = 7.1 Hz, 3-OH), 3.17 (1H, dq, *J* = 6.0, 6.9 Hz, H-6), 2.68 (3H, s, H-21), 2.54 (1H, ddd, *J* = 15.2, 8.1, 8.0 Hz, H-14a), 2.44 (1H, bs, 7-OH), 2.42 (1H, dd, *J* = 15.1, 2.9 Hz, H-2a), 2.41 (1H, ddd, *J* = 15.2, 2.3, 2.3 Hz, H-14b), 2.34 (1H, dd, *J* = 15.1, 10.8 Hz, H-2b), 2.20 (1H, m, H-10a), 2.18 (2H, m, H-11), 2.12 (1H, m, H-10b), 2.06 (3H, bs, H-27), 1.67 (3H, bs, H-25), 1.27 (3H, s, H-23), 1.21 (3H, d, *J* = 6.9 Hz, H-24), 1.15 (3H, s, H-22); $^{13}C$ NMR,

see Table 1; EIMS *m/z* 475 $[M]^+$ (6), 392 (7), 304 (6), 288 (33), 204 (76), 171 (19), 168 (100), 164 (12); HREIMS *m/z* 475.2380 (calcd. for $C_{26}H_{37}NO_5S$, 475.2392).

**Epothilone $D_5$ (23)**: colorless amorphous solid; $[\alpha]^{22}_D$ –150 (*c* 0.2, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 205 (23300), 248 (13600); IR (KBr) $\nu_{max}$ 3439, 2967, 2927, 1736, 1690, 1451, 1254, 1181, 987 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ; 6.94 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.34 (1H, bs, H-9), 5.29 (1H, dd, *J* = 8.0, 2.4 Hz, H-15), 5.16 (1H, dd, *J* = 8.2, 6.2 Hz, H-13), 4.30 (1H, bd, *J* = 4.9 Hz, H-7), 4.19 (1H, ddd, *J* = 10.8, 7.6, 3.0 Hz, H-3), 3.68 (1H, d, *J* = 7.6 Hz, 3-OH), 3.17 (1H, dq, *J* = 4.9, 7.0 Hz, H-6), 2.69 (3H, s, H-21), 2.65 (1H, d, *J* = 2.1 Hz, 7-OH), 2.56 (1H, ddd, *J* = 16.2, 8.2, 8.0 Hz, H-14a), 2.40 (1H, dd, *J* = 15.0, 3.0 Hz, H-2a), 2.39 (1H, bd, *J* = 16.2 Hz, H-14b), 2.34 (1H, dd, *J* = 15.0, 10.8 Hz, H-2b), 2.25 (2H, m, H-10a and H-11a), 2.20 (1H, m, H-10b), 2.17 (1H, m, H-11b), 2.05 (3H, d, *J* = 1.0 Hz, H-27), 1.69 (3H, bs, H-25), 1.68 (3H, bs, H-26), 1.29 (3H, s, H-23), 1.23 (3H, d, *J* = 7.0 Hz, H-24), 1.16 (3H, s, H-22); $^{13}C$ NMR, see Table 1; EIMS *m/z* 489 $[M]^+$ (4), 406 (4), 338 (7), 302 (13), 218 (35), 171 (10), 168 (100), 153 (20), 125 (10); HREIMS *m/z* 489.2536 (calcd. for $C_{27}H_{39}NO_5S$, 489.2549).

**Epothilone $C_6$ (24)**: colorless amorphous solid; $[\alpha]^{22}_D$ –205.2 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 218 (24600), 237 (28800); IR (KBr) $\nu_{max}$ 3435, 2967, 2927, 2882, 1732, 1688, 1465, 1258, 988 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.97 (1H, s, H-19), 6.58 (1H, bs, H-17), 6.43 (1H, dd, 15.5, 10.8 Hz, H-11), 6.11 (1H, dd, *J* = 10.8, 10.6 Hz, H-12), 5.75 (1H, ddd, *J* = 15.5, 8.3, 5.6 Hz, H-10), 5.34 (1H, m, H-13), 5.34 (1H, dd, *J* = 9.7, 2.4 Hz, H-15), 4.16 (1H, ddd, *J* = 9.2, 4.9, 4.3 Hz, H-3), 3.74 (1H, ddd, *J* = 2.2, 2.1, 1.7 Hz, H-7), 3.24 (1H, dq, *J* = 2.1, 6.9 Hz, H-6), 3.06 (1H, d, *J* = 2.2 Hz, 7-OH), 2.93 (1H, d, *J* = 4.9 Hz, 3-OH), 2.78 (1H, dddd,

*J* = 14.1, 9.9 9.7, 0.7, H-14a), 2.71 (3H, s, H-21), 2.48 (1H, m, H-9a), 2.47 (1H, dd, *J* = 15.5, 9.2 Hz, H-2a), 2.40 (1H, dd, *J* = 15.5, 4.3 Hz, H-2b), 2.38 (1H, bdd, *J* = 14.1, 7.8 Hz, H-14b), 2.11 (3H, d, *J* = 1.3 Hz, H-27), 1.96 (1H, m, H-8), 1.33 (3H, s, H-23), 1.11 (3H, d, *J* = 6.9 Hz, H-24), 1.06 (3H, s, H-22), 1.05 (3H, d, *J* = 6.8 Hz, H-25); $^{13}$C NMR, see Table 1; EIMS *m/z* 475 $[M]^+$ (13), 387 (2), 316 (4), 288 (15), 230 (16), 204 (9), 171 (18), 168 (100), 164 (14), 151 (17); HREIMS *m/z* 475.2361 (calcd. for $C_{26}H_{37}NO_5S$, 475.2392).

Epothilone $C_7$ (25): colorless amorphous solid; $[\alpha]_D^{22}$ –XXX (*c* 2.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) XXX (XXX), XXX (XXX); IR (KBr) $\nu_{max}$ XXX cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.01 (1H, s, H-19), 6.66 (1H, bs, H-17), 5.59 (1H, ddd, *J* = 11.1, 11.1, 3.8 Hz, H-12), 5.40 (1H, dd, *J* = 11.1, 9.2, H-13), 5.03 (1H, d, *J* = 9.3 Hz, H-15), 4.62 (1H, dd, *J* = 9.3, 9.2 Hz, H-14), 4.18 (1H, bd, *J* = 11.0 Hz, H-3), 3.72 (1H, bs, H-7), 3.20 (1H, bs, 3-OH), 3.09 (1H, dq, *J* = 1.9, 6.8 Hz, H-6), 3.00 (1H, bs, 7-OH), 2.69 (3H, s, H-21), 2.47 (1H, dd, *J* = 14.8, 11.0 Hz, H-2a), 2.32 (1H, dd, *J* = 14.8, 2.6 Hz, H-2b), 2.27 (1H, m, H-11a), 2.19 (3H, bs, H-27), 2.13 (1H, m, H-11b), 1.76 (1H, m, H-8), 1.70 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.32 (3H, s, H-23), 1.23 (1H, m, H-9b), 1.21 (1H, m, H-10b), 1.18 (3H, d, *J* = 6.8 Hz, H-24), 1.08 (3H, s, H-22), 1.00 (3H, d, *J* = 6.9 Hz, H-25); EIMS *m/z* 493 $[M]^+$ XXX; HREIMS *m/z* 493.XXX (calcd. for $C_{26}H_{39}NO_6S$, 493.2498).

Epothilone $C_8$ (26): colorless amorphous solid; $[\alpha]^{22}_D$ –75.2 (*c* 2.5, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 210 (16800), 248 (17800); IR (KBr) $\nu_{max}$ 3443, 2932, 2881, 1734, 1689, 1465, 1255, 1183, 976 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz) δ 6.93 (1H, s, H-19), 6.62 (1H, dd, *J* = 15.6, 0.6 Hz, H-17), 6.49 (1H, dd, *J* = 15.6, 6.6 Hz, H-16), 5.52 (1H, dddd, *J* = 9.5, 6.6, 2.8, 0.6 Hz, H-

15), 5.42 (1H, m, H-12), 5.41 (1H, m, H-13), 4.13 (1H, ddd, $J$ = 11.0, 5.3, 2.8 Hz, H-3), 3.69 (1H, ddd, $J$ = 3.7, 2.8, 2.5 Hz, H-7), 3.11 (1H, dq, $J$ = 2.5, 6.8 Hz, H-6), 2.95 (1H, d, $J$ = 5.3 Hz, 3-OH), 2.90 (1H, d, $J$ = 2.8 Hz, 7-OH), 2.69 (3H, s, H-21), 2.67 (1H, ddd, $J$ = 14.9, 9.5, 8.4 Hz, H-14a), 2.48 (1H, dd, $J$ = 15.6, 11.0 Hz, H-2a), 2.33 (1H, dd, $J$ = 15.6, 2.8 Hz, H-2b), 2.30 (1H, bd, $J$ = 14.9 Hz, H-14b), 2.14 (1H, m, H-11a), 2.03 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.31 (1H, m, H-9a), 1.29 (3H, s, H-23), 1.17 (3H, d, $J$ = 6.8 Hz, H-24), 1.16 (1H, m, H-10b), 1.14 (1H, m, H-9b), 1.05 (3H, s, H-22), 0.97 (3H, d, $J$ = 7.1 Hz, H-25); $^{13}$C NMR, see Table 1; EIMS *m/z* 463 $[M]^+$ (21), 310 (10), 276 (21), 171 (83), 154 (100), 150 (27), 111 (18); HREIMS *m/z* 463.2382 (calcd. for $C_{25}H_{37}NO_5S$, 463.2392).

**Epothilone $C_9$ (27):** colorless amorphous solid; $[\alpha]^{22}_D$ –93.4 (*c* 1.0, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 209 (15200), 254 (15700); IR (KBr) $\nu_{max}$ 3416, 2966, 2932, 1736, 1689, 1463, 1249, 1011 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.06 (1H, s, H-19), 6.65 (1H, bs, H-17), 6.56 (1H, dd, $J$ = 10.6, 4.4 Hz, 27-OH), 5.55 (1H, d, $J$ = 6.2 Hz, 3-OH),5.52 (1H, dd, $J$ = 11.6, 2.0 Hz, H-15), 5.44 (1H, dddd, $J$ = 11.2, 10.7, 3.1, 1.7 Hz, H-12), 5.35 (1H, dddd, $J$ = 11.0, 10.7, 3.9, 1.7 Hz, H-13), 4.47 (1H, ddd, $J$ = 12.5, 4.4, 1.3 Hz, H-27a), 4.35 (1H, ddd, $J$ = 11.7, 6.2, 2.6 Hz, H-3), 4.20 (1H, ddd, $J$ = 12.5, 10.6, 0.9 Hz, H-27b), 3.63 (1H, ddd, $J$ = 4.6, 1.8, 0.9 Hz, H-7), 3.24 (1H, d, $J$ = 1.8 Hz, 7-OH), 3.13 (1H, dq, $J$ = 0.9, 6.8 Hz, H-6), 2.80 (1H, ddd, $J$ = 14.8, 11.6, 11.0 Hz, H-14a), 2.71 (3H, s, H-21), 2.40 (1H, dd, $J$ = 14.4, 11.7 Hz, H-2a), 2.24 (1H, m, H-11a), 2.06 (1H, dd, $J$ = 14.4, 2.6 Hz, H-2b), 2.01 (1H, ddd, $J$ = 14.8, 3.9, 2.0 Hz, H-14b), 2.00 (1H, m, H-11b), 1.77 (1H, m, H-8), 1.69 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.35 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.19 (3H, d, $J$ = 6.8 Hz, H-24), 1.18 (1H, m, H-9b), 1.01 (3H, d, $J$ =

7.1 Hz, H-25), 0.98 (3H, s, H-22); $^{13}$C NMR, see Table 1; EIMS *m/z* 493 $[M]^+$ (17), 306 (64), 184 (50), 171 (30), 167 (38), 166 (100), 138 (12); HREIMS *m/z* 493.2502 (calcd. for $C_{26}H_{39}NO_6S$, 493.2498).

**trans-Epothilone $C_1$ (28):** colorless amorphous solid; $[\alpha]^{22}_D$ –84 (*c* 0.2, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 211 (17400), 248 (12900); IR (KBr) $\nu_{max}$ 3433, 2961, 2933, 2879, 1730, 1708, 1457, 1251, 975 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 600 MHz) δ 7.00 (1H, s, H-19), 6.64 (1H, bs, H-17), 5.45 (1H, ddd, *J* = 15.2, 6.5, 6.5 Hz, H-12), 5.42 (1H, dd, *J* = 6.4, 3.7 Hz, H-15), 5.35 (1H, dt, *J* = 15.2, 7.1 Hz, H-13), 4.42 (1H, m, H-3), 3.58 (1H, ddd, *J* = 8.1, 7.9, 2.8 Hz, H-7), 3.24 (1H, m, H-6), 3.14 (1H, dq, *J* = 4.0, 6.9 Hz, H-6), 2.92 (1H, d, *J* = 7.9 Hz, 7-OH), 2.71 (3H, s, H-21), 2.71 (2H, m, H-2), 2.53 (2H, m, H-14), 2.17 (1H, d, *J* = 2.17 Hz, 3-OH), 2.11 (1H, m, H-11a), 2.06 (3H, bs, H-27), 1.93 (1H, m, H-11b), 1.68 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-8), 1.26 (3H, d, *J* = 6.8 Hz, H-24), 1.16 (1H, m, H-10b), 1.12 (3H, d, *J* = 6.9 Hz, H-22), 1.07 (1H, m, H-9b), 1.00 (3H, d, *J* = 6.8 Hz, H-25); $^{13}$C NMR, see Table 1; EIMS *m/z* 463 $[M]^+$ (6), 290 (21), 289 (20), 204 (23), 194 (19), 190 (22), 168 (100), 164 (48), 157 (14), 152 (19), 151 (17), 139 (15), 111 (18); HREIMS *m/z* 463.2371 (calcd. for $C_{25}H_{37}NO_5S$, 463.2392).

**trans-Epothilone $C_2$ (29):** colorless amorphous solid; $[\alpha]^{22}_D$ –3 (*c* 1.5, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 211 (15800), 248 (11900); IR (KBr) $\nu_{max}$ 3435, 2963, 2931, 2878, 1731, 1706, 1457, 1273, 979 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 600 MHz) δ 6.99 (1H, s, H-19), 6.57 (1H, bs, H-17), 5.56 (1H, ddd, *J* = 15.1, 7.4, 7.0 Hz, H-12), 5.41 (1H, ddd, *J* = 15.1, 7.0, 6.9 Hz, H-13), 5.41 (1H, dd, *J* = 7.7, 2.8 Hz, H-15), 4.13 (1H, dddd, *J* = 6.7, 6.2, 5.6, 5.1 Hz, H-3), 3.78 (1H, ddd, *J* = 8.2, 6.5, 1.9 Hz, H-7), 3.18 (1H, d, *J* = 5.6 Hz, 3-OH), 3.06 (1H, dq, *J* = 8.2, 7.1 Hz,

H-6), 2.98 (1H, dq, *J* = 6.2, 7.0 Hz, H-4), 2.71 (3H, s, H-21), 2.64 (1H, dd, *J* = 15.1, 6.7 Hz, H-2a), 2.54 (1H, dd, *J* = 15.1, 5.1 Hz, H-2b), 2.44 (2H, m, H-14), 2.22 (1H, dddd, *J* = 13.8, 7.0, 6.2, 2.9 Hz, H-11a), 2.10 (3H, d, *J* = 1.1 Hz, H-27), 2.09 (1H, d, *J* = 6.5 Hz, 7-OH), 1.88 (1H, dddd, *J* = 13.8, 10.9, 7.4, 2.9 Hz, H-11b), 1.65 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.56 (1H, dddd, *J* = 12.7, 12.7, 3.9, 3.9 Hz, H-9a), 1.20 (3H, d, *J* = 7.1 Hz, H-24), 1.15 (3H, d, *J* = 7.0 Hz, H-23), 1.13 (1H, m, H-10b), 1.04 (1H, m, H-9b), 1.01 (3H, d, *J* = 7.0 Hz, H-25); $^{13}$C NMR, see Table 1; EIMS *m/z* 463 $[M]^+$ (13), 290 (11), 190 (10), 168 (100), 164 (20), 157 (26), 139 (17); HREIMS *m/z* 463.2383 (calcd. for $C_{25}H_{37}NO_5S$, 463.2392).

**Epothilone $I_1$ (30)**: colorless amorphous solid; $[\alpha]_D^{22}$ **–XXX (*c* XXX, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) XXX; IR (KBr) $\nu_{max}$ XXX cm$^{-1}$;** $^1$H NMR ($CDCl_3$, 300 MHz) δ 6.96 (1H, s, H-19), 6.54 (1H, bs, H-17), 5.49 (1H, ddd, *J* = 10.3, 7.3, 7.3 Hz, H-12), 5.33 (1H, dd, *J* = 8.3, 4.4 Hz, H-15), 5.31 (1H, m, H-13), 4.15 (1H, ddd, *J* = 8.0, 5.0, 4.6 Hz, H-3), 3.80 (1H, m, H-7), 3.21 (1H, dq, *J* = 6.0, 6.9 Hz, H-6), 2.89 (1H, d, *J* = 5.0 Hz, 3-OH); 2.70 (3H, s, H-21), 2.65 (1H, ddd, *J* = 15.8, 8.5, 8.3 Hz, H-14a), 2.42 (2H, m, H-2), 2.35 (1H, m, H-14b), 2.27 (1H, bd, *J* = 3.3 Hz, 7-OH), 2.13 (1H, m, H-11a), 2.09 (3H, d, *J* = 1.2 Hz, H-27), 2.00 (1H, m, H-11b), 1.72 (1H, m, H-8), 1.40 (2H, m, H-10$_\beta$), 1.37 (1H, m, H-9$_\beta$a), 1.36 (2H, m, H-9$_\alpha$), 1.32 (3H, s, H-23), 1.27 (3H, m, H-9$_\beta$b and H-10$_\alpha$), 1.13 (3H, d, *J* = 6.9 Hz, H-24), 1.09 (3H, s, H-22), 0.94 (3H, d, *J* = 6.9 Hz, H-25); $^{13}$C NMR ($CDCl_3$, 75 MHz) δ 221.3 (s, C-5), 171.1 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.4 (s, C-16), 133.8 (d, C-12), 124.6 (d, C-13), 120.0 (d, C-17), 116.2 (d, C-19), 78.8 (d, C-15), 74.9 (d, C-7), 74.7 (d, C-3), 51.6 (s, C-4), 43.7 (d, C-6), 38.9 (t, C-2), 34.3 (d, C-8), 31.6 (t, C-14), 29.3 (t, C-9$_\alpha$), 28.6 (t, C-10$_\beta$), 28.2 (t, C-10$_\alpha$), 26.6 (t, C-

11), 24.8 (t, C-9$_\beta$), 23.6 (q, C-22), 19.3 (q, C23), 19.3 (q, C-21), 16.5 (q, C-25), 15.5 (q, C-27), 13.7 (q, C-24); EIMS *m/z* 505 $[M]^+$ XXX; HREIMS *m/z* 505.XXX (calcd. for $C_{28}H_{43}NO_5S$, 505.XXX).

Epothilone $I_2$ (31): colorless amorphous solid; $[\alpha]_D^{22}$ –XXX (*c* XXX, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) XXX; IR (KBr) $\nu_{max}$ XXX $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.40 (1H, m, H-12), 5.38 (1H, dd, *J* = 9.8, 3.3 Hz, H-15), 5.37 (1H, m, H-13), 4.21 (1H, ddd, *J* = 8.6, 3.8, 3.6 Hz, H-3), 3.85 (1H, ddd, *J* = 8.5, 5.8, 2.2 Hz, H-7), 3.18 (1H, dq, *J* = 8.5, 7.0 Hz, H-6), 2.70 (3H, s, H-21), 2.65 (1H, ddd, *J* = 15.2, 9.8, 9.0 Hz, H-14a), 2.51 (1H, d, *J* = 3.6 Hz, 3-OH), 2.37 (2H, m, H-2), 2.32 (1H, bd, *J* = 15.2 Hz, H-14b), 2.09 (3H, d, *J* = 1.3 Hz, H-27), 2.07 (2H, m, H-11), 1.78 (1H, m, H-8), 1.65 (1H, d, *J* = 5.8 Hz, 7-OH), 1.57 (1H, m, H-10$_\beta$a), 1.44 (1H, m, H-10$_\alpha$a), 1.42 (1H, m, H-9$_\beta$), 1.32 (3H, s, H-23), 1.21 (1H, m, H-10$_\beta$b), 1.17 (3H, d, *J* = 7.0 Hz, H-24), 1.13 (2H, m, H-9$_\alpha$), 1.06 (3H, s, H-22), 0.95 (3H, d, *J* = 7.0 Hz,H-25$_\alpha$), 0.91 (3H, d, *J* = 6.5 Hz, H-25$_\beta$), 0.68 (1H, m, H-10$_\alpha$b); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ 220.4 (s, C-5), 171.3 (s, C-1), XXX (s, C-20), 152.4 (s, C-18), 137.6 (s, C-16), 134.5 (d, C-12), 125.3 (d, C-13), 119.6 (d, C-17), 116.2 (d, C-19), 78.6 (d, C-15), 77.2 (d, C-7), 75.0 (d, C-3), 51.0 (s, C-4), 44.6 (d, C-6), 38.2 (t, C-2), 36.9 (t, C-9$_\alpha$), 34.5 (t, C-10$_\alpha$), 32.6 (d, C-8), 32.0 (t, C-14), 30.0 (d, C-9$_\beta$), 27.4 (t, C-11), 26.6 (t, C-10$_\beta$), 25.0 (q, C-22), 21.5 (q, C-25$_\beta$), 19.3 (q, C-21), 17.9 (q, C-25$_\alpha$), 17.7 (q, C-23), 15.8 (q, C-24), 15.6 (q, C-27); EIMS *m/z* 519 $[M]^+$ XXX; HREIMS *m/z* 519.XXX (calcd. for $C_{29}H_{45}NO_5S$, 519.XXX).

Epothilone $I_3$ (32): colorless amorphous solid; $[\alpha]_D^{22}$ –XXX (*c* XXX, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) XXX; IR (KBr) $\nu_{max}$ XXX $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 6.95 (1H,

s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd, $J$ = 9.1, 3.0 Hz, H-15), 5.08 (1H, dd, $J$ = 8.5, 3.9 Hz, H-13), 4.13 (1H, ddd, $J$ = 9.4, 4.3, 3.2 Hz, H-3), 3.81 (1H, m, H-7), 3.18 (1H, dq, $J$ = 6.8, 7.0 Hz, H-6), 2.83 (1H, d, $J$ = 4.3 Hz, 3-OH), 2.70 (3H, s, H-21), 2.61 (1H, ddd, $J$ = 15.8, 9.1, 8.5 Hz, H-14a), 2.43 (1H, dd, $J$ = 14.0, 3.2 Hz, H-2a), 2.38 (2H, dd, $J$ = 14.0, 9.4 Hz, H-2b), 2.30 (1H, bd, $J$ = 15.8 Hz, H-14b), 2.16 (1H, ddd, $J$ = 14.1, 8.3, 7.4 Hz, H-11a), 2.08 (3H, d, $J$ = 1.0 Hz, H-27), 1.99 (1H, d, $J$ = 4.7 Hz, 7-OH), 1.92 (1H, ddd, $J$ = 14.1, 6.3, 6.3 Hz, H-11b), 1.82 (1H, m, H-8), 1.67 (3H, s, H-26), 1.51 (1H, m, H-10$_\beta$a), 1.40 (1H, m, H-9$_\beta$), 1.33 (1H, m, H-10$_\beta$b), 1.31 (3H, s, H-23), 1.27 (1H, m, H-10$_\alpha$a), 1.23 (1H, m, H-9$_\alpha$a), 1.16 (3H, d, $J$ = 7.0 Hz, H-24), 1.10 (1H, m, H-9$_\alpha$b), 1.07 (3H, s, H-22), 0.95 (3H, d, $J$ = 7.0 Hz,H-25$_\alpha$), 0.92 (3H, d, $J$ = 6.5 Hz, H-25$_\beta$), 0.75 (1H, m, H-10$_\alpha$b); **EIMS *m/z* 533 [M]$^+$ XXX; HREIMS *m/z* 533.XXX (calcd. for $C_{30}H_{47}NO_5S$, 533.XXX).**

**Epothilone $I_4$ (33):** colorless amorphous solid; **$[\alpha]_D^{22}$ –XXX (*c* XXX, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) XXX; IR (KBr) $\nu_{max}$ XXX cm$^{-1}$;** $^1$H NMR ($CDCl_3$, 400 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.47 (1H, dt, $J$ = 11.1, 5.8 Hz, H-12), 5.33 (1H, ddd, $J$ = 9.2, 3.9, 0.5 Hz, H-15), 5.33 (1H, m, H-13), 4.09 (1H, dddd, $J$ = 9.6, 8.1, 4.5, 3.3 Hz, H-3), 3.83 (1H, m, H-7), 3.57 (1H, bs, 3-OH), 2.89 (1H, dq, $J$ = 7.4, 7.1 Hz, H-6), 2.83 (1H, dq, $J$ = 8.1, 7.1 Hz, H-4), 2.70 (3H, s, H-21), 2.64 (1H, m, H-14a), 2.42 (1H, dd, $J$ = 14.2, 3.3 Hz, H-2a), 2.43 (1H, dd, $J$ = 14.2, 9.6 Hz, H-2b), 2.30 (1H, m, H-14b), 2.10 (3H, d, $J$ = 1.3 Hz, H-27), 2.09 (2H, m, H-11), 1.81 (1H, m, H-8), 1.74 (1H, bd, $J$ = 5.6 Hz, 7-OH), 1.53 (1H, m, H-10$_\beta$a), 1.49 (1H, m, H-9$_\beta$), 1.47 (1H, m, H-10$_\alpha$a), 1.27 (1H, m, H-10$_\beta$b), 1.24 (1H, m, H-9$_\alpha$a), 1.17 (3H, d, $J$ = 7.1 Hz, H-23), 1.14 (1H, m, H-9$_\alpha$b), 1.08 (3H, d, $J$ = 7.1 Hz, H-24), 0.97 (3H, d, $J$ = 6.9 Hz,H-25$_\alpha$),

0.91 (3H, d, $J$ = 6.5 Hz, H-25$_\beta$), 0.79 (1H, m, H-10$_\alpha$b); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 217.0 (s, C-5), 170.8 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.1 (s, C-16), 134.6 (d, C-12), 124.7 (d, C-13), 120.2 (d, C-17), 116.4 (d, C-19), 78.7 (d, C-15), 76.4 (d, C-7), 71.3 (d, C-3), 50.7 (d, C-4), 50.1 (d, C-6), 40.7 (t, C-2), 38.5 (t, C-9$_\alpha$), 35.5 (t, C-10$_\alpha$), 33.4 (d, C-8), 31.8 (t, C-14), 30.0 (d, C-9$_\beta$), 27.2 (t, C-11), 26.7 (t, C-10$_\beta$), 21.4 (q, C-25$_\beta$), 19.3 (q, C-21), 18.2 (q, C-25$_\alpha$), 15.4 (q, C-27), 14.4 (q, C-24), 13.1 (q, C-23); EIMS *m/z* 505 $[M]^+$ XXX; HREIMS *m/z* 505.XXX (calcd. for $C_{28}H_{43}NO_5S$, 505.XXX).

**Epothilone $I_5$ (34)**: colorless amorphous solid; $[\alpha]_D^{22}$ –XXX (*c* XXX, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) XXX; IR (KBr) $\nu_{max}$ XXX cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 6.97 (1H, s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd, $J$ = 7.1, 6.2 Hz, H-15), 5.03 (1H, dd, $J$ = 8.4, 5.0 Hz, H-13), 4.05 (1H, dddd, $J$ = 7.5, 7.2, 5.9, 4.6 Hz, H-3), 3.91 (1H, m, H-7), 3.17 (1H, d, $J$ = 5.9 Hz, 3-OH), 2.94 (1H, dq, $J$ = 7.2, 7.1 Hz, H-4), 2.87 (1H, dq, $J$ = 6.5, 6.9 Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd, $J$ = 14.6, 4.6 Hz, H-2a), 2.60 (1H, m, H-14a), 2.53 (1H, dd, $J$ = 14.6, 7.5 Hz, H-2b), 2.31 (1H, m, H-14b), 2.10 (3H, d, $J$ = 1.1 Hz, H-27), 2.10 (1H, m, H-11a), 2.02 (1H, m, H-11b), 1.97 (1H, bd, $J$ = 5.6 Hz, 7-OH), 1.84 (1H, m, H-8), 1.66 (3H, s, H-26), 1.55 (1H, m, H-9$_\beta$), 1.49 (1H, m, H-10$_\beta$a), 1.39 (1H, m, H-10$_\beta$b), 1.33 (1H, m, H-10$_\alpha$a), 1.31 (1H, m, H-9$_\alpha$a), 1.15 (3H, d, $J$ = 7.1 Hz, H-23), 1.12 (1H, m, H-9$_\alpha$b), 1.11 (3H, d, $J$ = 6.9 Hz, H-24), 0.97 (3H, d, $J$ = 6.9 Hz,H-25$_\alpha$), 0.94 (1H, m, H-10$_\alpha$b), 0.93 (3H, d, $J$ = 6.6 Hz, H-25$_\beta$); EIMS *m/z* 519 $[M]^+$ XXX; HREIMS *m/z* 519.XXX (calcd. for $C_{29}H_{45}NO_5S$, 519.XXX).

**Epothilone $I_\epsilon$ (35)**: colorless amorphous solid; $[\alpha]_D^{22}$ –XXX (*c* XXX, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) XXX; IR (KBr) $\nu_{max}$ XXX cm$^{-1}$;$^1$H NMR ($CDCl_3$, 400 MHz) δ 6.97 (1H,

s, H-19), 6.52 (1H, bs, H-17), 5.24 (1H, dd, $J$ = 6.9, 6.9 Hz, H-15), 5.02 (1H, dd, $J$ = 8.8, 5.2 Hz, H-13), 4.22 (1H, tdd, $J$ = 6.1, 5.6, 4.8 Hz, H-3), 3.76 (1H, ddd, $J$ = 6.1, 5.7, 5.6 Hz, H-7), 3.13 (1H, d, $J$ = 5.6 Hz, 3-OH), 3.05 (1H, dq, $J$ = 4.8, 7.0 Hz, H-4), 2.79 (1H, dq, $J$ = 5.6, 6.9 Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, m, H-14a), 2.57 (2H, d, $J$ = 6.1 Hz, H-2a), 2.30 (1H, m, H-14b), 2.08 (3H, d, $J$ = 1.0 Hz, H-27), 2.02 (2H, m, H-11), 1.73 (1H, d, $J$ = 6.1 Hz, 7-OH), 1.69 (1H, m, H-8), 1.66 (3H, s, H-26), XXX (H-$9_\alpha$, H-$9_\beta$, H-$10_\alpha$, H-$10_\beta$), 1.21 (3H, d, $J$ = 7.0 Hz, H-22), 1.16 (3H, d, $J$ = 6.9 Hz, H-24), 0.94 (3H, d, $J$ = 6.9 Hz,H-$25_\alpha$), 0.91 (3H, d, $J$ = 6.4 Hz, H-$25_\beta$); EIMS *m/z* 519 $[M]^+$ XXX; HREIMS *m/z* 519.XXX (calcd. for $C_{29}H_{45}NO_5S$, 519.XXX).

**Epothilone K (36):** colorless amorphous solid; $[\alpha]^{22}_D$ –7 (*c* 0.08, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 212 (16700), 248 (12500); IR (KBr) $\nu_{max}$ 3431, 2963, 2927, 2856, 1731, 1712, 1262, 1093, 1021, 802 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.95 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.49 (3H, m, H-15, H-13, and H-12), 4.04 (1H, dddd, $J$ = 7.9, 7.6, 6.9, 3.3 Hz, H-3), 3.36 (1H, dq, $J$ = 6.9, 6.8 Hz, H-6), 2.83 (1H, d, $J$ = 7.6 Hz, 3-OH), 2.75 (1H, ddd, $J$ = 16.1, 6.6, 3.4 Hz, H-14a), 2.74 (1H, dd, $J$ = 15.3, 3.3 Hz, H-2a), 2.71 (3H, s, H-21), 2.58 (2H, m, H-14b and H-8), 2.50 (1H, dd, $J$ = 15.3, 7.9 Hz, H-2b), 2.29 (1H, m, H-11a), 2.10 (1H, m, H-11b), 2.09 (3H, d, $J$ = 0.7 Hz, H-27), 1.78 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.48 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.15 (3H, d, $J$ = 6.8 Hz, H-22), 1.03 (3H, d, $J$ = 6.5 Hz, H-25); EIMS *m/z* 405 $[M]^+$ (38), 317 (12), 260 (9), 232 (10), 204 (14), 190 (16), 168 (100), 164 (30), 151 (28); HREIMS *m/z* 405.XXX (calcd. for $C_{26}H_{39}NO_5S$, 405.XXX).

(37): colorless amorphous solid; $[\alpha]^{22}_D$ –27.5 (*c* 0.4, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε)

211 (16100), 247 (12100); IR (KBr) $\nu_{max}$ 3431, 2967, 2929, 2875, 1704, 1462, 1381, 1010 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.56 (1H, dtt, *J* = 10.8, 7.3, 1.4 Hz, H-12), 5.39 (1H, dtt, *J* = 10.8, 7.3, 1.4 Hz, H-13), 4.17 (1H, t, *J* = 6.6 Hz, H-15), 3.50 (1H, ddd, *J* = 8.7, 2.6, 2.6 Hz, H-7), 3.10 (1H, d, *J* = 2.6, 7-OH), 2.90 (1H, dq, *J* = 2.6, 7.2 Hz, H-6), 2.77 (1H, sep, *J* = 6.9 Hz, H-4), 2.70 (3H, s, H-21), 2.40 (2H, m, H-14), 2.07 (2H, m, H-11), 2.04 (3H, d, *J* = 1.1 Hz, H-27), 1.78 (1H, bs, 15-OH), 1.74 (1H, m, H-9a), 1.50 (1H, m, H-8), 1.46 (1H, m, H-10a), 1.27 (1H, m, H-10b), 1.11 (1H, m, H-9b), 1.094 (3H, d, *J* = 6.9 Hz, H-23), 1.089 (3H, d, *J* = 6.9 Hz, H-22), 1.08 (3H, d, *J* = 7.2 Hz, H-24), 0.82 (3H, d, *J* = 6.7 Hz, H-25); $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ 220.5 (s, C-5), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 133.4 (d, C-12), 125.0 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 74.9 (d, C-7), 44.9 (d, C-6), 40.0 (d, C-4), 35.5 (d, C-8), 33.5 (t, C-14), 32.3 (t, C-9), 27.9 (t, C-11), 26.9 (t, C-10), 19.2 (q, C-21), 18.6 (q, C-23), 18.1 (q, C-22), 15.6 (q, C-25), 14.4 (q, C-27), 9.3 (q, C-24); EIMS *m/z* 407 $[M]^+$ (0.1), 204 (0.8), 168 (100), 140 (3.4); **HREIMS *m/z* 407.XXX (calcd. for $C_{23}H_{37}NO_3S$, 407.XXX).**

**(38)**: colorless amorphous solid; $[\alpha]^{22}_D$ +25.0 (*c* 0.5, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 212 (17700), 247 (13400); IR (KBr) $\nu_{max}$ 3427, 2971, 2933, 2878, 2858, 1709, 1457, 1377, 1186, 1023 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) δ 6.95 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.52 (1H, dtt, *J* = 10.9, 7.2, 1.4 Hz, H-12), 5.39 (1H, dtt, *J* = 10.9, 7.1, 1.2 Hz, H-13), 4.18 (1H, ddt, *J* = 3.4, 0.4, 6.7 Hz, H-15), 2.71 (3H, s, H-21), 2.51 (1H, bq, *J* = 6.8 Hz, H-8), 2.48 (1H, dq, *J* = 17.7, 7.4 Hz, H-6a), 2.41 (1H, dq, *J* = 17.7, 7.2 Hz, H-6b), 2.39 (2H, ddd, *J* = 7.1, 6.7, 1.4 Hz, H-14), 2.06 (2H, ddt, 7.2, 1.2, 7.0 Hz, H-11), 2.05 (3H, d, *J* = 1.4 Hz, H-27), 1.81 (1H, d, *J* = 3.4 Hz,

15-OH), 1.66 (1H, m, H-9a), 1.32 (1H, m, H-9b), 1.31 (2H, m, H-10), 1.06 (3H, d, $J$ = 6.9 Hz, H-25), 1.04 (3H, dd, $J$ = 7.4, 7.2 Hz, H-24); $^{13}$C NMR ($CDCl_3$, 75 MHz) δ 215.3 (s, C-7), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 132.7 (d, C-12), 125.3 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 46.0 (d, C-8), 34.3 (t, C-14), 33.5 (t, C-6), 32.7 (t, C-9), 27.5 (t, C-11), 27.3 (t, C-10), 19.2 (q, C-21), 16.5 (q, C-25), 14.4 (q, C-27), 7.8 (q, C-24); EIMS *m/z* 335 $[M]^+$ (2), 317 (4), 170 (27), 169 (67), 168 (100), 140 (20); HREIMS *m/z* 335.1912 (calcd. for $C_{19}H_{29}NO_2S$, 335.1919).

(39): colorless amorphous solid; $[\alpha]^{22}_D$ +26.4 (*c* 0.27, MeOH); UV (MeOH) $\lambda_{max}$ nm (ε) 203 (19100), 244 (12500); IR (KBr) $\nu_{max}$ 3430, 2970, 2934, 2877, 1710, 1458, 1377, 1184 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.17 (1H, t, $J$ = 7.3 Hz, H-13), 4.13 (1H, m, H-15), 2.70 (3H, s, H-21), 2.51 (1H, bq, $J$ = 6.8 Hz, H-8), 2.47 (1H, dq, $J$ = 17.7, 7.2 Hz, H-6a), 2.41 (1H, dq, $J$ = 17.7, 7.2 Hz, H-6b), 2.33 (2H, bdd, $J$ = 7.3, 6.8 Hz, H-14), 2.05 (3H, d, $J$ = 1.2 Hz, H-27), 2.03 (2H, m, H-11), 1.71 (1H, d, $J$ = 3.2 Hz, 15-OH), 1.69 (3H, d, $J$ = 1.3 Hz, H-26), 1.62 (1H, m, H-9a), 1.32 (3H, m, H-10 and H-9b), 1.06 (3H, d, $J$ = 6.9 Hz, H-25), 1.03 (3H, t, $J$ = 7.2 Hz, H-24); EIMS *m/z* 349 $[M]^+$ (0.7), 331 (1.7), 168 (100), 140 (5.1); HREIMS *m/z* 349.XXX (calcd. for $C_{20}H_{31}NO_2S$, 349.XXX).

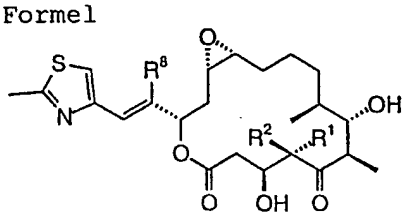
Tab 1. Aktivität von Epothilonen und Verbindungen (1) bis (39) gegen Maus-Fibroblasten (L929, IC50 /ng/ml/)

| Struktur-typ | Epothilone | | | | |
|---|---|---|---|---|---|
| | $A_Y$ | $B_Y$ | $C_Y$ | $D_Y$ | trans $C_Y$ |
| Ausgangs-epothilon | (1) 4 | (2) 1-2 | (14) 50-100 | (15) 20 | - |
| 21-Hydroxy (E&F) | (3) 10 | (4) 1.5 | - | - | - |
| Oxazoles (G&H) | (10) 6 | (11) 1 | (12) 120 | (13) 11 | - |
| *(R)*-4-Desmethyl ($X_1$) | (5) 20 | - | (16) 200 | (17) 20 | (28) 400 |
| *(S)*-4-Desmethyl ($X_2$) | (6) 7 | - | (18) 25-30 | (19) 12 | (29) 80 |
| 6-Desmethyl ($X_3$) | - | - | (20) 1500 | - | - |
| 8-Desmethyl ($X_4$) | - | - | (21) 800 | - | - |
| 8,9-Dehydro ($X_5$) | - | - | (22) 1500 | (23) 200 | - |
| 10,11-Dehydro ($X_6$) | - | - | (24) 120 | - | - |
| 14-Hydroxy ($X_7$) | - | - | (25) | - | - |
| 16-Desmethyl ($X_8$) | (7) 20 | - | (26) 250 | - | - |
| 27-Hydroxy ($X_9$) | (8) 100 | - | (27) 200 | - | - |
| 21-Methyl ($X_{10}$) | - | (9) 1.5 | - | - | - |
| Verbindung | - | - | (36) 180 | | |
| Verbindung | - | - | (37) 50 | - | - |
| Verbindung | - | - | (38) 2000 | (39) 500 | - |

Epothilon-Nebenkomponenten

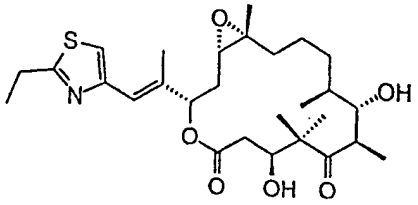
Patentansprüche

1. Epothilon der Formel



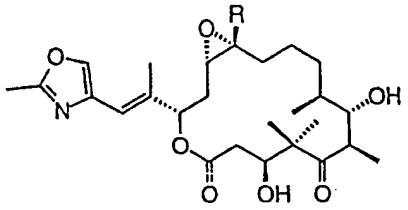
Epothilone $A_1$ (5) $R^1 = H$; $R^2, R^8 = Me$
Epothilone $A_2$ (6) $R^2 = H$; $R^1, R^8 = Me$
Epothilone $A_8$ (7) $R^8 = H$; $R^1, R^2 = Me$ oder
Epothilone $A_9$ (8) $R^1 = CH_2OH$; $R^2, R^8 = Me$

2. Epothilon der Formel



Epothilone $B_{10}$ (9)

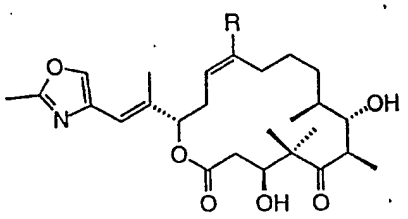
3. Epothilon der Formel



- ✓ Epothilone $G_1$ **(10)** R = H
- ✓ Epothilone $G_2$ **(11)** R = Me

oder

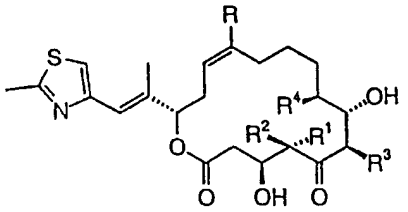
4. Epothilon der Formel



- ✓ Epothilone $H_1$ **(12)** R = H
- ✓ Epothilone $H_2$ **(13)** R = Me

oder

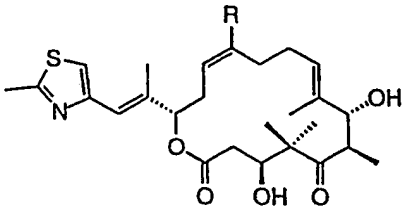
5. Epothilon der Formel



- ✓ Epothilone $C_1$ **(16)** $R^1$ = H; $R^2$, $R^3$, $R^4$ = Me; R = H
- ✓ Epothilone $D_1$ **(17)** $R^1$ = H; $R^2$, $R^3$, $R^4$ = Me; R = Me
- ✓ Epothilone $C_2$ **(18)** $R^2$ = H; $R^1$, $R^3$, $R^4$ = Me; R = H
- ✓ Epothilone $D_2$ **(19)** $R^2$ = H; $R^1$, $R^3$, $R^4$ = Me; R = Me
- ✓ Epothilone $C_3$ **(20)** $R^3$ = H; $R^1$, $R^2$, $R^4$ = Me; R = H
- ✓ Epothilone $C_4$ **(21)** $R^4$ = H; $R^1$, $R^2$, $R^3$ = Me; R = H

oder

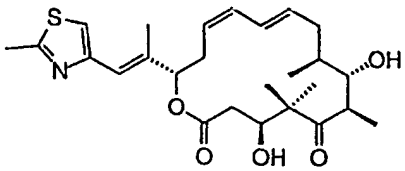
6. Epothilon der Formel



Epothilone $C_5$ (22) R = H
Epothilone $D_5$ (23) R = Me

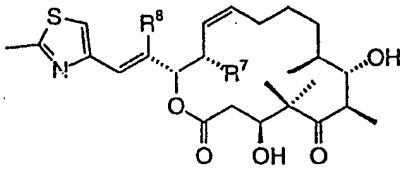
oder

7. Epothilon der Formel



✓ Epothilone $C_6$ (24)

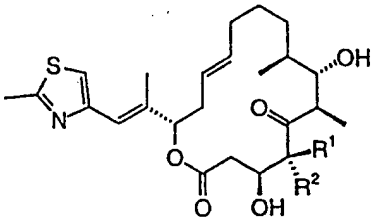
8. Epothilin der Formel



✓ Epothilone $C_7$ (25) $R^7$ = OH; $R^8$ = Me
✓ Epothilone $C_8$ (26) $R^8$, $R^7$ = H
✓ Epothilone $C_9$ (27) $R^8$ = $CH_2OH$; $R^7$ = H

oder

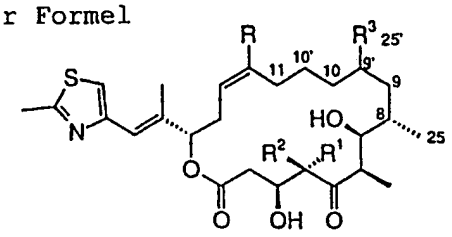
9. Epothilon der Formel



✓ trans-Epothilone $C_1$ (28) $R^1$ = H; $R^2$ = Me
✓ trans-Epothilone $C_2$ (29) $R^2$ = H; $R^1$ = Me

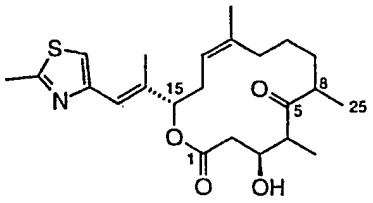
oder

10. Epothilon der Formel



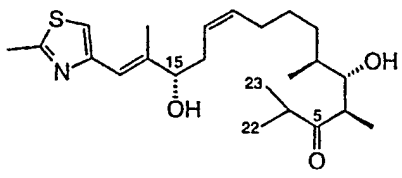
Epothilone $I_1$ (30) R, $R^3$ = H; $R^1$, $R^2$ = Me
Epothilone $I_2$ (31) R = H; $R^1$, $R^2$, $R^3$ = Me
Epothilone $I_3$ (32) $R^1$, $R^2$, $R^3$, R = Me
Epothilone $I_4$ (33) $R^2$, R = H; $R^1$, $R^3$ = Me
Epothilone $I_5$ (34) $R^2$ = H; $R^1$, $R^3$, R = Me oder
Epothilone $I_6$ (35) $R^1$ = H; $R^2$, $R^3$, R = Me

11. Epothilon der Formel



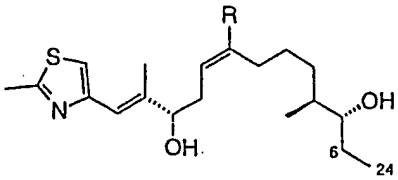
Epothilone K (36)

12. Verbindung der Formel



(37)

13. Verbindung der Formel



(38) R = H oder
(39) R = Me

**Fig. 1** Trennungsgang für Rohepothilone

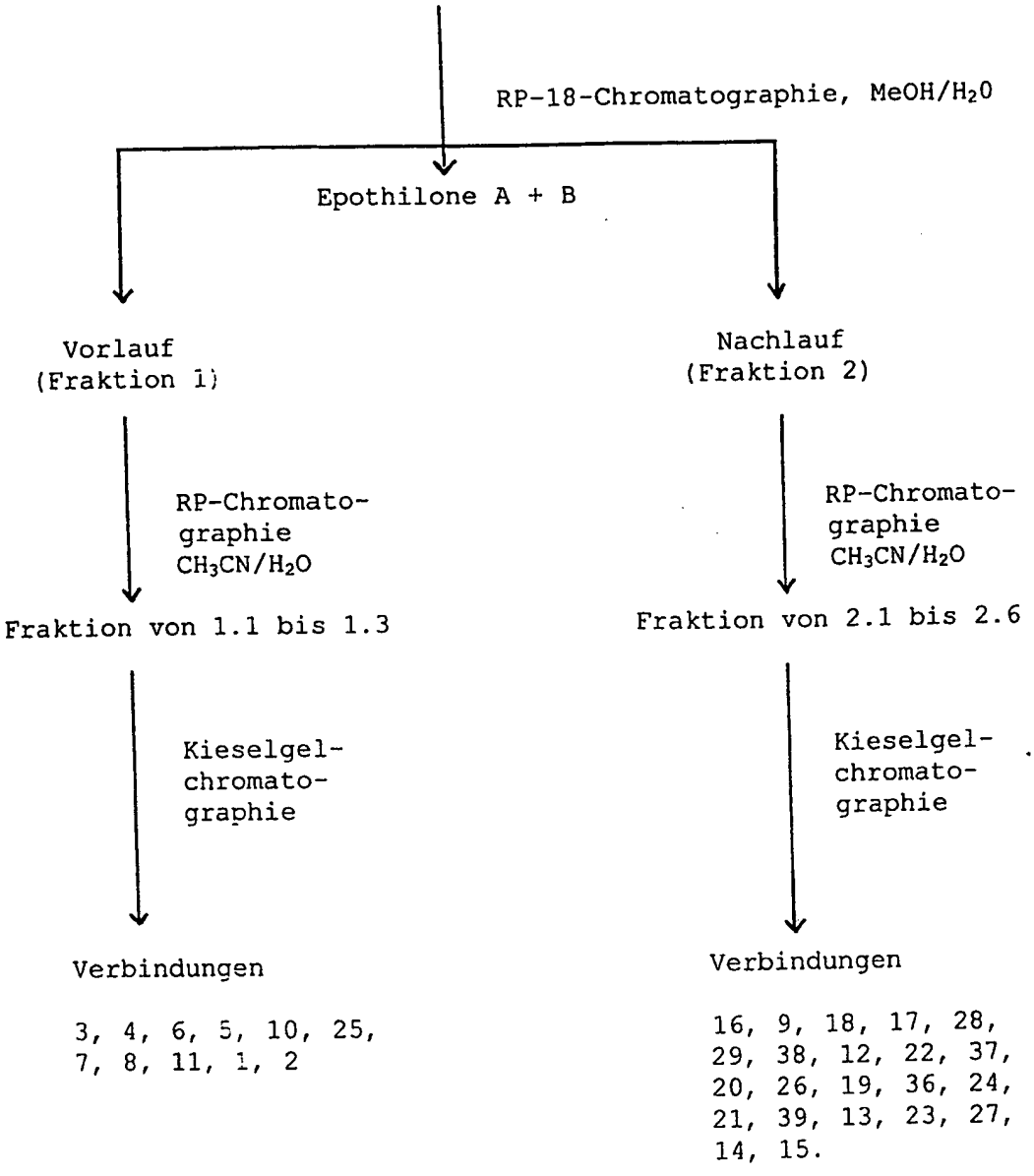
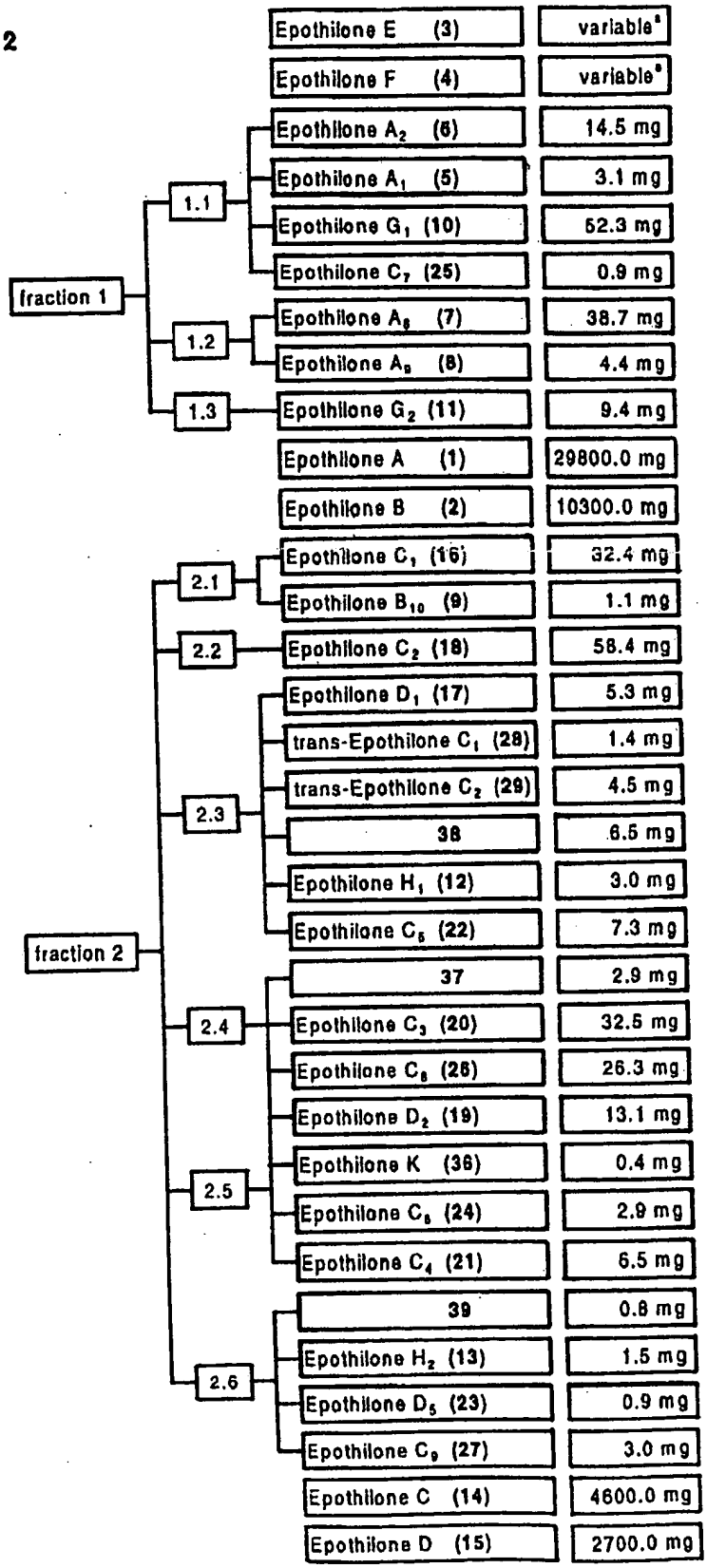


Fig. 2


fraction 1
1.1
1.2
1.3
fraction 2
2.1
2.2
2.3
2.4
2.5
2.6
Epothilone E (3)
variable*
Epothilone F (4)
variable*
Epothilone A2 (6)
14.5 mg
Epothilone A1 (5)
3.1 mg
Epothilone G1 (10)
52.3 mg
Epothilone C7 (25)
0.9 mg
Epothilone A6 (7)
38.7 mg
Epothilone A5 (8)
4.4 mg
Epothilone G2 (11)
9.4 mg
Epothilone A (1)
29800.0 mg
Epothilone B (2)
10300.0 mg
Epothilone C1 (16)
32.4 mg
Epothilone B10 (9)
1.1 mg
Epothilone C2 (18)
58.4 mg
Epothilone D1 (17)
5.3 mg
trans-Epothilone C1 (28)
1.4 mg
trans-Epothilone C2 (29)
4.5 mg
38
6.5 mg
Epothilone H1 (12)
3.0 mg
Epothilone C5 (22)
7.3 mg
37
2.9 mg
Epothilone C3 (20)
32.5 mg
Epothilone C6 (26)
26.3 mg
Epothilone D2 (19)
13.1 mg
Epothilone K (36)
0.4 mg
Epothilone C5 (24)
2.9 mg
Epothilone C4 (21)
6.5 mg
39
0.8 mg
Epothilone H2 (13)
1.5 mg
Epothilone D5 (23)
0.9 mg
Epothilone C9 (27)
3.0 mg
Epothilone C (14)
4600.0 mg
Epothilone D (15)
2700.0 mg

**PCT** WELTORGANISATION FÜR GEISTIGES EIGENTUM
Internationales Büro

INTERNATIONALE ANMELDUNG VERÖFFENTLICHT NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)

(51) Internationale Patentklassifikation 6 :
**C07D 493/04, 417/06, 413/06, 277/24**
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A3

(11) Internationale Veröffentlichungsnummer: **WO 99/65913**

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(30) Prioritätsdaten:
198 26 988.9 18. Juni 1998 (18.06.98) DE

(71) Anmelder *(für alle Bestimmungsstaaten ausser US)*: GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH (GBF) [DE/DE]; Mascheroder Weg 1, D–38124 Braunschweig (DE).

(72) Erfinder; und
(75) Erfinder/Anmelder *(nur für US)*: HOEFLE, Gerhard [DE/DE]; Mascheroder Weg 1, D–38124 Braunschweig (DE). REICHENBACH, Hans [DE/DE]; Mascheroder Weg 1, D–38124 Braunschweig (DE). GERTH, Klaus [DE/DE]; Mascheroder Weg 1, D–38124 Braunschweig (DE). HARDT, Ingo [DE/DE]; Mascheroder Weg 1, D–38124 Braunschweig (DE). SASSE, Florenz [DE/DE]; Mascheroder Weg 1, D–38124 Braunschweig (DE). STEINMETZ, Heinrich [DE/DE]; Mascheroder Weg 1, D–38124 Braunschweig (DE).

(74) Anwälte: BOETERS, Hans usw.; Boeters & Bauer, Bereiteranger 15, D–81541 München (DE).

(81) Bestimmungsstaaten: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO Patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Veröffentlicht**
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(88) Veröffentlichungsdatum des internationalen Recherchenberichts: 20. April 2000 (20.04.00)

(54) Title: EPOTHILONE MINOR CONSTITUENTS

(54) Bezeichnung: EPOTHILON–NEBENKOMPONENTEN

(57) Abstract

The invention relates to compounds which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans–epothilones C1 and C2.

(57) Zusammenfassung

Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 und K und Trans–Epothilone C1 und C2.

*LEDIGLICH ZUR INFORMATION*

Codes zur Identifizierung von PCT-Vertragsstaaten auf den Kopfbögen der Schriften, die internationale Anmeldungen gemäss dem PCT veröffentlichen.

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# INTERNATIONAL SEARCH REPORT

Internation Application No
PCT/EP 99/04244

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D493/04 C07D417/06 C07D413/06 C07D277/24
//(C07D493/04,313:00,303:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

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IPC 6 C07D

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | WO 98 08849 A (NOVARTIS AKTIENGESELLSCHAFT ;BAUER ARMIN (DE); CORDES MARTIN (DE);) 5 March 1998 (1998-03-05) abstract; claims; examples | 1-13 |
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| X | WO 97 19086 A (BIOTECHNOLOG FORSCHUNG GMBH ;KIFFE MICHAEL (DE); HOEFLE GERHARD (D) 29 May 1997 (1997-05-29) abstract; claims; examples | 1-13 |

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|---|---|
| 22 February 2000 | 07/03/2000 |

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|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016 | Paisdor, B |

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| Internation ,pplication No |
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| PCT/EP 99/04244 |

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| Category * | Citation of document, with indication,where appropriate, of the relevant passages | Relevant to claim No. |
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Internatio. Aktenzeichen
PCT/EP 99/04244

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
IPK 6 C07D493/04 C07D417/06 C07D413/06 C07D277/24
//(C07D493/04,313:00,303:00)

Nach der Internationalen Patentklassifikation (IPK) oder nach der nationalen Klassifikation und der IPK

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C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

| Kategorie* | Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile | Betr. Anspruch Nr. |
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[X] Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen

[X] Siehe Anhang Patentfamilie

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| X | SU D -S ET AL: "STRUCTURE - ACTIVITY RELATIONSHIPS OF THE EPOTHILONES AND THE FIRST IN VIVO COMPARISON WITH PACLITAXEL" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION,DE,VERLAG CHEMIE. WEINHEIM, Bd. 36, Nr. 19, 1997, Seiten 2093-2096, XP002916075 ISSN: 0570-0833 Seite 2094 -Seite 2095 | 1-13 |

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Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
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| | | EP 0923583 A | 23-06-1999 |
| | | US 5969145 A | 19-10-1999 |
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| | | CZ 9901750 A | 15-09-1999 |
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